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L5 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
2005:182920 Document No. 142:258503 Secreted polypeptide species in **human** plasma, detection assays for smaller proteins and tryptic peptides, and expression profiles useful for disease diagnosis. Argoud-puy, Guilaine; Bederr, Nassima; Bougueleret, Lydie; Cusin, Isabelle; Mahe, Eve; Niknejad, Anne; Reffas, Samia; Rose, Keith; Saudrais, Cedric; Scherer, Andreas; Papoian, Ruben; Dengler, Uwe Jochen; Croft, Laurence James (Genova Ltd., Bermuda; Novartis Ag; Novartis Pharma GmbH). PCT Int. Appl. WO 2005019825 A2 20050303, 284 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-EP9323 20040819. PRIORITY: US 2003-2003/PV496966 20030820.

AB The invention relates to polypeptide species secreted in **human** plasma, isolated polynucleotides encoding such polypeptides, polymorphic variants thereof, and the use of said nucleic acids and polypeptides or compns. thereof for detection assays and disease diagnosis. An industrial-scale method, involving sample pooling, is detailed for the anal. of smaller proteins (mol. weight less than about 40 kDa and mostly under 20 kDa),a nd thousands of peptides resulting from polypeptides can be identified from a single pool. Low abundance proteins such as leptin and ghrelin and peptides such as bradykinin, were clearly identified. By identifying the actual plasma polypeptide species, differences in mRNA processing and splicing, translation rate, mRNA stability, and

posttranslational modifications are revealed, and plasma localization points to a novel, previously unknown function for the polypeptides of the invention. Peptides corresponding to 3 specific **human** plasma polypeptides (HPP) were identified and selected for functional characterization: esophageal cancer-related gene 2 (ECRG2), thymosin β4, and pancreastatin. Treatment of mice with these three HPP species resulted in gene expression profiles showing that these proteins would be useful in diagnosis treatment of cancer or hyperplasia-associated conditions, neurodegeneration or ion balance-associated diseases, and diseases associated with dysregulated serum glucose (e.g., diabetes) or metabolic disorders (e.g., amyloidosis).

L5 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
2005:572337 Document No. 143:92107 Peroxisome-associated **peroxiredoxin 5**, nucleotide sequence encoding said polypeptide and their uses in the diagnosis and/or the treatment of lung injuries and diseases, and of oxidative stress-related disorders. Knoops, Bernard; Hermans, Cedric; Bernard, Alfred; Wattiez, Ruddy; Flamagne, Paul; Plaisant, Frank; Gressens, Pierre; Murrell, George A. G.; Wang, Min-Xia (Belg.). U.S. Pat. Appl. Publ. US 2005142126 A1 20050630, 38 pp., Cont.-in-part of U.S. Ser. No. 486,167. (English). CODEN: USXXCO. APPLICATION: US 2003-686157 20031015. PRIORITY: BE 1997-692 19970820; WO 1998-BE124 19980820; US 2000-2000/486167 20000815.
AB A **human** peroxisome-associated polypeptide (designated **peroxiredoxin 5** or **PRDX5**) and its corresponding genomic DNA and cDNA sequence encoding the peroxisome-associated polypeptide are disclosed. **Human PRDX5** cDNA contains two ATG initiation codons, giving a long or a short **PRDX5** form; the short form contains a peroxisomal targeting signal type 1 and is localized to peroxisomes, the cytosol and the nucleus, whereas the long form has mitochondrial localization due to the presence of a mitochondrial targeting sequence which is absent in the sort form. The corresponding nucleotide and amino acid sequence from rat and mouse **PRDX5** are also provided. **PRDX5** is up-regulated by H2O2 and inflammatory cytokines for protection against oxidative stress, and plays a role in inflammatory and pneumotoxic reactions, as well as protects against excitotoxic brain lesions. The protein is useful in the diagnosis and/or treatment of several diseases, particularly lung injuries and diseases as well as oxidative stress-related disorders, particularly neurotoxic injury or excitotoxic injury.

L5 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
2005:497362 Document No. 143:42267 Genes induced in brain by exposure to β-amyloid peptides and the development of drug targets for treatment of Alzheimer's disease. Gan, Li; Gonzalez-Zulueta, Mirella; Ye, Shiming; Urfer, Roman; Nikolich, Karoly (AGY Therapeutics, Inc., USA). U.S. Pat. Appl. Publ. US 2005123962 A1 20050609, 131 pp. (English). CODEN: USXXCO. APPLICATION: US 2004-974148 20041026. PRIORITY: US 2003-2003/PV515536 20031028.
AB This invention provides a method for detecting a neurodegenerative disorder or susceptibility to a neurodegenerative disorder in a subject by identifying genes showing altered levels of expression in response to the disease. Specifically, genes induced by exposure to toxic peptides derived from β-amyloid are identified as markers for Alzheimer's disease and the gene products are identified as potential drug targets. Also included in the present invention is a method reducing toxic Aβ peptide production by a eukaryotic cell, and a method of ameliorating neurotoxicity of the peptide. The present invention further embodies compns. such as Alzheimer's Disease-associated genes, the polypeptides encoded therefrom, gene delivery vehicles, host cells and kits comprising the Alzheimer's Disease-associated genes and/or polypeptides. Genes induced by β-amyloid in hippocampus or cortex in a mouse Alzheimer's disease model were identified by subtractive hybridization. Genes induced in rat by injection of β-amyloid peptides into the hippocampus were also

identified.

L5 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
2005:394682 Document No. 142:445550 Gene expression profiles for the diagnosis and prognosis of breast cancer. Erlander, Mark; Ma, Xiao-Jun; Wang, Wei; Wittliff, James L. (Arcturus Bioscience, Inc. University of Louisville, USA). U.S. Pat. Appl. Publ. US 2005095607 A1 20050505, 40 pp. (English). CODEN: USXXCO. APPLICATION: US 2004-795092 20040305. PRIORITY: US 2003-2003/PV453006 20030307.
AB The invention relates to the identification and use of gene expression profiles, or patterns, suitable for identification of breast cancer patient populations with different survival outcomes. The gene expression profiles may be embodied in nucleic acid expression, protein expression, or other expression formats, and may be used in the study and/or determination of the prognosis of a patient, including breast cancer survival.

L5 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
2005:1078815 Document No. 143:434432 Crystal structures of oxidized and reduced forms of **human** mitochondrial thioredoxin 2. meets, Aude; Evrard, Christine; Landtmeters, Marie; Marchand, Cecile; Knoops, Bernard; Declercq, Jean-Paul (Unit of Structural Chemistry (CSTR), Institut des Sciences de la Vie, Universite catholique de Louvain, Louvain-la-Neuve, B-1348, Belg.). Protein Science, 14(10), 2610-2621 (English) 2005. CODEN: PRCIEI. ISSN: 0961-8368. Publisher: Cold Spring Harbor Laboratory Press.
AB Mammalian thioredoxin 2 is a mitochondrial isoform of highly evolutionary conserved thioredoxins. Thioredoxins are small ubiquitous protein-disulfide oxidoreductases implicated in a large variety of biol. functions. In mammals, thioredoxin 2 is encoded by a nuclear gene and is targeted to mitochondria by a N-terminal mitochondrial presequence. Recently, mitochondrial thioredoxin 2 (TXN2) was shown to interact with components of the mitochondrial respiratory chain and to play a role in the control of mitochondrial membrane potential, regulating mitochondrial apoptosis signaling pathway. Here we report the first crystal structures of a mammalian mitochondrial thioredoxin 2. Crystal forms of reduced and oxidized **human** thioredoxin 2 are described at 2.0 and 1.8 Å resolution Though the folding is rather similar to that of **human** cytosolic/nuclear thioredoxin 1, important differences are observed during the transition between the oxidized and the reduced states of **human** thioredoxin 2, compared with **human** thioredoxin 1. In spite of the absence of the Cys residue implicated in dimer formation in **human** thioredoxin 1, dimerization still occurs in the crystal structure of **human** thioredoxin 2, mainly mediated by hydrophobic contacts, and the dimers are associated to form two-dimensional polymers. Interestingly, the structure of **human** thioredoxin 2 reveals possible interaction domains with **human peroxiredoxin 5** (**PRDX5**), a substrate protein of **human** thioredoxin 2 in mitochondria.

L5 ANSWER 6 OF 17 MEDLINE on STN DUPLICATE 1
2005065732. PubMed ID: 15695408. Immunogenicity without immunoselection: a mutant but functional antioxidant enzyme retained in a **human** metastatic melanoma and targeted by CD8(+) T cells with a memory phenotype. Sensi Marialuisa; Nicolini Gabriella; Zanon Marina; Colombo Chiara; Molla Alessandra; Bersani Ilaria; Lupetti Raffaella; Parmiani Giorgio; Anichini Andrea. (Units of Immunobiology of Human Tumors, Department of Experimental Oncology, Istituto Nazionale per lo Studio e la Cura dei Tumori, Via Venezian 1, Milan, Italy.. marialuisa.sensi@istitutotumori.mi.it) . Cancer research, (2005 Jan 15) 65 (2) 632-40. Journal code: 2984705R. ISSN: 0008-5472. Pub. country: United States. Language: English.
AB **Human** melanomas can express unique tumor antigens, resulting from mutated proteins, and shared epitopes encoded for by normal genes, but these two classes of antigens have not been previously compared for

immunogenicity and retention in metastatic cells. Here, we identified a new unique antigen generated by a point mutation in the **peroxiredoxin 5** (**Prdx5**) gene in an HLA-A*0201(+) **human** metastatic melanoma lacking the wild-type allele. An antioxidant assay, with recombinant **Prdx5** proteins, and evaluation of peroxide accumulation in transiently transfected cells, indicated that the mutant protein retained its enzymatic activity. The mutation in the **Prdx5** protein did not generate a new HLA agretope but yielded an HLA-A*0201-restricted T cell epitope ( **Prdx5**(110-119)). By HLA-tetramer analysis, in a tumor-invaded lymph node, >50% of mutant **Prdx5**-specific CD8(+) T cells (frequency 0.37%/CD8(+)) showed a CCR7(+/-) CD45RA(-) "T(CM)" or "T(EM)" phenotype, as found in Melan-A/MART-1-specific T cells (frequency 0.68%/CD8(+)) in the same tissue. In agreement with their memory phenotype, the **Prdx5**-specific T cells readily expanded in vitro in mixed lymphocyte-tumor culture, as did the Melan-/MART-1-specific T cells. By immunohistochemistry of the invaded lymph node, the mutant **Prdx5** protein was expressed in all neoplastic cells, in contrast with the heterogeneous expression of shared antigens as Melan-A/MART-1, gp100 and tyrosinase. Thus, a unique tumor antigen can be as immunogenic as the melanoma differentiation antigens but, in contrast to the latter, may be retained in all metastatic cells possibly as result of the relevant cellular function exerted by the mutated protein.

L5 ANSWER 7 OF 17 MEDLINE on STN DUPLICATE 2

2005153168. PubMed ID: 15785239. **Peroxiredoxin 5** expression in the **human** thyroid gland. Gerard A-C; Many M-C; Daumerie Ch; Knoops B; Colin I M. (Unite de Morphologie Experimentale, B-1200, Bruxelles, Belgium. ) Thyroid : official journal of the American Thyroid Association, (2005 Mar) 15 (3) 205-9. Journal code: 9104317. ISSN: 1050-7256. Pub. country: United States. Language: English.

AB **Peroxiredoxin 5** (**PRDX5**) is a newly discovered thioredoxin peroxidase able to reduce peroxides that is implicated in antioxidant protective mechanisms. We report here its expression in the **human** thyroid gland. Twenty-seven **human** thyroid specimens were examined by immunohistochemistry. They included six normal thyroid tissues, five multinodular goiters, nine hot nodules, two Hurthle cell adenomas, and five thyroids from patients with Graves' disease. In the control tissue, **PRDX5** expression was heterogeneous, being stronger in cubical functionally active follicular cells than in flat quiescent thyrocytes. It was diffuse in the cytoplasm, occasionally localized in inclusions that most likely corresponded to mitochondria. This feature was particularly marked in the Hurthle cell adenoma case. In multinodular goiters, hot nodules, and Graves' thyroids, the cytosolic labeling was enhanced compared to the control tissue and a signal was also detected in few nuclei. To determine whether the level of expression was different between multinodular goiters and hyperthyroid Graves' thyroids, **PRDX5** immunoblotting was performed in these two respective tissues. We observed that **PRDX5** expression was higher in the thyroid gland of patients with Graves' disease compared to multinodular goiters. In conclusion, our data show that **PRDX5** is expressed in the thyroid gland where it could act as antioxidant. The level of expression is directly correlated with the functional status of epithelial cells, being higher in multinodular goiters, and even more pronounced in hyperthyroid tissues, such as Graves' disease.

L5 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

2004:240530 Document No. 140:419858 Crystal Structure of a Dimeric Oxidized form of **Human Peroxiredoxin 5.** Evrard, Christine; Capron, Arnaud; Marchand, Cecile; Clippe, Andre; Wattiez, Ruddy; Soumillion, Patrice; Knoops, Bernard; Declercq, Jean-Paul (Unit of Structural Chemistry (CSTR), Universite Catholique de Louvain, Louvain-la-Neuve, B-1348, Belg.). Journal of Molecular Biology, 337(5), 1079-1090 (English) 2004. CODEN: JMOBAK. ISSN: 0022-2836. Publisher:

Elsevier.

AB **Peroxiredoxin 5** (**PRDX5**) is the last discovered mammalian member of an ubiquitous family of peroxidases widely distributed among prokaryotes and eukaryotes. Mammalian **peroxiredoxin 5** has been recently classified as an atypical 2-Cys peroxiredoxin due to the presence of a conserved peroxidatic N-terminal cysteine (Cys47) and an unconserved resolving C-terminal cysteine residue (Cys151) forming an intramol. disulfide intermediate in the oxidized enzyme. We have recently reported the crystal structure of **human peroxiredoxin 5** in its reduced form. Here, a new crystal form of **human peroxiredoxin 5** is described at 2.0 Å resolution The asym. unit contains three polypeptide chains. Surprisingly, beside two reduced chains, the third one is oxidized although the enzyme was crystallized under initial reducing conditions in the presence of 1 mM 1,4-dithio-DL-threitol. The oxidized polypeptide chain forms an homodimer with a symmetry-related one through intermol. disulfide bonds between Cys47 and Cys151. The formation of these disulfide bonds is accompanied by the partial unwinding of the N-terminal parts of the α2 helix, which in the reduced form contains the peroxidatic Cys47 and the α6 helix, which is sequentially close to the resolving residue Cys151. In each monomer of the oxidized chain, the C-terminal part including the α6 helix is completely reorganized and is isolated from the rest of the protein on an extended arm. In the oxidized dimer, the arm belonging to the first monomer now appears at the surface of the second subunit and vice versa.

L5 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

2004:770314 Document No. 142:129690 Crystal structure of the C47S mutant of **human peroxiredoxin 5.** Evrard, Christine; Smeets, Aude; Knoops, Bernard; Declercq, Jean-Paul (Unit of Structural Chemistry, Universite catholique de Louvain, Louvain-la-Neuve, B-1348, Belg.). Journal of Chemical Crystallography, 34(8), 553-558 (English) 2004. CODEN: JCCYEV. ISSN: 1074-1542. Publisher: Springer Science+Business Media, Inc..

AB In the crystal structure of the reduced form of the wild-type **human peroxiredoxin 5** (**PRDX5**), the presence of a benzoate ion in direct interaction with the peroxidatic Cys-47 residue appeared as a rather intriguing feature since it is known that the benzoate ion can play the role of a specific hydroxyl radical scavenger. Here, the crystal structure of the C47S mutant of **human PRDX5** was crystallized in the tetragonal system, space group P41212, with a = 65.65 Å and c = 122.04 Å. It confirms the presence of this benzoate ion in spite of the mutation to Ser of the Cys-47 residue to which the benzoate ion was directly linked in the wild-type structure. The benzoate ion appeared to be stabilized by hydrophobic contacts on both sides of the aromatic ring. In this matter, the α5 helix, which was specific to **PRDX5** among mammalian PRDXs, played an important role. These hydrophobic contacts also allowed the authors to suggest why the benzoate ion disappears when the mol. is oxidized.

L5 ANSWER 10 OF 17 MEDLINE on STN DUPLICATE 3

2004372414. PubMed ID: 15276323. Overexpression of antioxidant enzyme **peroxiredoxin 5** protects **human** tendon cells against apoptosis and loss of cellular function during oxidative stress. Yuan Jun; Murrell George A C; Trickett Annette; Landtmeters Marie; Knoops Bernard; Wang Min-Xia. (Orthopaedic Research Institute, St. George Hospital Campus, 4-10 South Street, University of New South Wales, Sydney, NSW 2217, Australia. ) Biochimica et biophysica acta, (2004 Jul 23) 1693 (1) 37-45. Journal code: 0217513. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.

AB Oxidative stress and apoptosis are implicated in tendon degeneration. **Peroxiredoxin 5** (**PRDX5**) is a novel thioredoxin peroxidase recently identified in mammals, participating directly in

eliminating hydrogen peroxide (H(2)O(2)) and neutralizing other reactive oxygen species (ROS). We have previously reported that **PRDX5** is upregulated in degenerative **human** tendon. However, the effects of this upregulation on **human** tendon cell function remain unknown, in particular, with regards to oxidative stress conditions. Here we report that exposure of **human** tendon cells to 50 microM H(2)O(2) for 24 h (in vitro oxidative stress) caused a significant increase in the percentage of apoptotic cells ($P<0.05$) as assessed by flow cytometric analysis of Annexin V binding, accompanied by increased PRXD5 mRNA and protein expression. Overexpression of **PRDX5** in **human** tendon cells via transfection inhibited H(2)O(2)-induced tendon cell apoptosis by 46% ($P<0.05$), and prevented the decrease in tendon cell collagen synthesis which occurs under H(2)O(2) challenge, although the decrease in collagen synthesis was small. Results from our study indicate that the antioxidant enzyme **PRDX5** plays a protective role in **human** tendon cells against oxidative stress by reducing apoptosis and maintaining collagen synthesis.

L5 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
2003:967377 Document No. 140:230218 Cloning of bovine peroxiredoxins-gene expression in bovine tissues and amino acid sequence comparison with rat, mouse and primate peroxiredoxins. Leyens, Gregory; Donnay, Isabelle; Knoops, Bernard (Institut des Sciences de la Vie, Unite des Sciences Veterinaires, Universite Catholique de Louvain, Louvain-la-Neuve, B-1348, Belg.). Comparative Biochemistry and Physiology, Part B: Biochemistry & Molecular Biology, 136B(4), 943-955 (English) 2003. CODEN: CBPBB8. ISSN: 1096-4959. Publisher: Elsevier.

AB The peroxiredoxin (PRDX) family is a recently identified family of peroxidases found in organisms ranging from bacteria to mammals. In mammals, six PRDX isoforms have been characterized in **human** (Homo sapiens), rat (Rattus norvegicus) and mouse (Mus musculus). PRDXs are cytosolic, secreted or targeted to organelles such as peroxisomes, mitochondria and the nucleus. Some PRDXs are synthesized as larger precursor proteins with a presequence that is cleaved to produce the mature form. To study the expression of the six PRDXs in bovine (Bos taurus), we first cloned cDNAs coding for PRDX1, PRDX2, PRDX4 and **PRDX5.** PRDX3 and PRDX6 had previously been cloned and characterized in bovine. The comparison of bovine PRDXs with their rat, mouse and primate orthologues reveals a min. of 95% similarity of mature proteins. Even though mitochondrial or export signal presequences are normally less conserved, the unprocessed proteins still present a min. of 84% similarity. Nevertheless, a major divergence lies at the N-terminus of bovine PRDX2, where a Cys-Val-Cys motif was identified. The expression of the six PRDXs in 22 bovine tissues has been studied by RT-PCR. Our results point out the ubiquity of the different PRDX transcripts in bovine tissues. The important conservation of the different PRDXs, the multiple processes they have been associated with, as well as the ubiquity of all the members of the family analyzed in this study for the first time altogether, suggest that they play a major role in the basal metabolism of mammalian cells.

L5 ANSWER 12 OF 17 MEDLINE on STN DUPLICATE 4
2003148414. PubMed ID: 12654475. Recombinant **peroxiredoxin 5** protects against excitotoxic brain lesions in newborn mice. Plaisant Frank; Clippe Andre; Vander Stricht Delphine; Knoops Bernard; Gressens Pierre. (INSERM E 9935 and Service de Neurologie Pediatrique, Hopital Robert-Debre, Paris, France. ) Free radical biology & medicine, (2003 Apr 1) 34 (7) 862-72. Journal code: 8709159. ISSN: 0891-5849. Pub. country: United States. Language: English.

AB The pathophysiology of brain lesions associated with cerebral palsy is multifactorial and likely involves excess release of glutamate and excess production of free radicals, among other factors. Theoretically, antioxidants could limit the severity of these brain lesions. Peroxiredoxins are a family of peroxidases widely distributed in eukaryotes and prokaryotes. **Peroxiredoxin 5** (

**PRDX5**) is a recently discovered mammalian member of this family of antioxidant enzymes that is able to reduce hydrogen peroxide and alkyl hydroperoxides. The present study was designed to examine the neuroprotective effects of recombinant **PRDX5** against neonatal excitotoxic challenge in both in vivo and in vitro experiments. For in vivo experiments, mice (postnatal day 5) were injected intraneopallially with ibotenate acting on NMDA and metabotropic receptors, or S-bromowillardiine acting on AMPA-kainate receptors to produce excitotoxic stress and brain lesions. Systemically administered recombinant **PRDX5** provided protection against ibotenate-induced excitotoxic stress. Brain lesions of animals given ibotenate and **PRDX5** were up to 63% smaller than that given ibotenate alone. However, **PRDX5** provided no prevention from lesions induced with S-bromowillardiine. A mutated recombinant **PRDX5** that is devoid of peroxidase activity was also tested and showed no protection against lesions induced by either ibotenate or S-bromowillardiine. Two classical antioxidants, N-acetylcysteine and catalase-PEG, provided the same neuroprotective effect as **PRDX5.** For in vitro experiments, neocortical neurons were exposed to 300 microM NMDA alone, NMDA plus recombinant **PRDX5** , or NMDA, recombinant **PRDX5** and dithiothreitol, a classical electron donor for peroxiredoxins. Recombinant **PRDX5** plus dithiothreitol displayed a synergistic neuroprotective effect on NMDA-induced neuronal death. These findings indicate that reactive oxygen species production participates in the formation of NMDA receptor-mediated brain lesions in newborn mice and that antioxidant compounds, such as **PRDX5**, provide some neuroprotection in these models.

L5 ANSWER 13 OF 17 MEDLINE on STN DUPLICATE 5

2003015431. PubMed ID: 12522579. Identification of calcium-induced genes in HaCaT keratinocytes by polymerase chain reaction-based subtractive hybridization. Seo Eun-Young; Piao Yong-Jun; Kim Jeong-Soo; Suhr Ki-Beom; Park Jang-Kyu; Lee Jeung-Hoon. (Department of Dermatology, Chungnam University Hospital, Daesa-dong 640, Jung-gu, Daejeon 301-040, South Korea. ) Archives of dermatological research, (2002 Dec) 294 (9) 411-8. Electronic Publication: 2002-11-05. Journal code: 8000462. ISSN: 0340-3696. Pub. country: Germany: Germany, Federal Republic of. Language: English.

AB Suppression subtractive hybridization, a PCR-based method for cDNA subtraction, was used to identify differentially expressed genes in keratinocytes. Differentiation was induced by elevating the calcium level in the cell culture medium. Using HaCaT immortalized keratinocytes cultured in the presence of a high calcium concentration, we isolated 60 clones representing 48 different genes. By reverse Northern analysis, 13 genes were scored as overexpressed in these HaCaT cells. Northern blot analysis was used to confirm differential gene expression. Six genes, keratin 1, plasminogen activator inhibitor type 2 (PAI-2), ferritin H, **peroxiredoxin 5** (**PRDX5**), insulin-like growth factor binding protein-3 (IGFBP-3), and one EST gene, were differentially expressed in HaCaT cells cultured in the presence of a high calcium concentration. Two of these genes, keratin 1 and PAI-2, are differentially expressed during keratinocyte terminal differentiation. IGFBP-3, which has reduced expression during epidermal differentiation, was increased after culture in a high-calcium medium for 2 or 5 days. Overexpression of the ferritin H and **PRDX5** genes due to elevated calcium has not been reported in keratinocytes. We demonstrated the expression of IGFBP-3, ferritin H, **PRDX5**, and one gene of a matching sequence from the EST database during differentiation in primary cultured normal **human** keratinocytes. The EST gene expressed two transcripts of 1.8 kb and 2.5 kb in HaCaT cells, and the transcripts were confirmed to increase in keratinocytes cultured in a high-calcium medium.

L5 ANSWER 14 OF 17 MEDLINE on STN DUPLICATE 6

2002657506. PubMed ID: 12417342. Expression and regulation of **peroxiredoxin 5** in **human** osteoarthritis. Wang Min Xia; Wei Aiqun; Yuan Jun; Trickett Annette; Knoops Bernard; Murrell

George A C. (Orthopaedic Research Institute, St George Hospital, University of New South Wales, Sydney, NSW, Australia. ) FEBS letters, (2002 Nov 6) 531 (2) 359-62. Journal code: 0155157. ISSN: 0014-5793. Pub. country: Netherlands. Language: English.

AB Reactive oxygen species (ROS) are implicated in the pathogenesis of osteoarthritis (OA). However, little is known about the antioxidant defence system in articular cartilage. We investigated the expression and regulation of **peroxiredoxin 5** (**PRDX5**), a newly discovered thioredoxin peroxidase, in **human** normal and osteoarthritic cartilage. Our results show that **human** cartilage constitutively expresses **PRDX5.** Moreover, the expression is up-regulated in OA. Inflammatory cytokines tumour necrosis factor alpha and interleukin 1 beta contribute to this up-regulation by increasing intracellular ROS production. The present study suggests that **PRDX5** may play a protective role against oxidative stress in **human** cartilage.

L5 ANSWER 15 OF 17 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

2003:326944 Document No.: PREV200300326944. ANTIOXIDANT ENZYME **PEROXIREDOXIN 5** IS EXPRESSED AT LOWER LEVELS IN NEURONS VULNERABLE TO CELL DEATH IN ALZHEIMER'S DISEASE. Landtmeters, M. [Reprint Author]; Alzate, L. [Reprint Author]; Brion, J. P.; Knoops, B. [Reprint Author]. Laboratory of Cell Biology, Universit Catholique de Louvain, Louvain-la-Neuve, Belgium. Society for Neuroscience Abstract Viewer and Itinerary Planner, (2002) Vol. 2002, pp. Abstract No. 784.4. http://sfn.scholarone.com. cd-rom.
Meeting Info.: 32nd Annual Meeting of the Society for Neuroscience. Orlando, Florida, USA. November 02-07, 2002. Society for Neuroscience. Language: English.

AB **Peroxiredoxin 5** (**PRDX5**) is a peroxidase of the mitochondrial thioredoxin system which is thought to play a major protective role against oxidative damages. Many neurological disorders, including Alzheimers disease (AD), are associated with oxidative stress and mitochondria have been implicated in such a process. In AD, the hippocampus is one of the first region of the brain to develop neuropathological lesions and is, in advanced cases, an heavily affected area. To determine whether the vulnerability of certain neuronal populations of the hippocampus could be due to a less efficient protection by the mitochondrial thioredoxin system, we analyzed by immunohistochemistry the expression of **PRDX5** in the hippocampus of adults rats, of normal control **humans** and of AD patients. Our results show that **PRDX5** is well expressed in neurons of CA4 and CA2/3 sectors, and of the subiculum. However, **PRDX5** immunoreactivity was weak in neurons of the CA1 sector and of the dentate gyrus. In AD brains, **PRDX5** expression in CA1 decreased or was totally absent. Moreover, we tested in COS-7 cells the protection conferred by **PRDX5** overexpression against oxidative stress induced by peroxides. At 100 M tert-butyl hydroperoxide, high expression of **PRDX5** decreased significantly apoptotic cell death. These results suggest that high levels of **PRDX5** may play an important protective role against oxidative stress. We conclude that the vulnerability of certain neuronal populations of the hippocampus in AD could be partly due to a weak expression of **PRDX5.**

L5 ANSWER 16 OF 17 MEDLINE on STN DUPLICATE 7

2001475436. PubMed ID: 11518528. Crystal structure of **human peroxiredoxin 5**, a novel type of mammalian peroxiredoxin at 1.5 A resolution. Declercq J P; Evrard C; Clippe A; Stricht D V; Bernard A; Knoops B. (Universite Catholique de Louvain, Unit of Structural Chemistry (CSTR), 1 place Louis Pasteur, Louvain-la-Neuve, B-1348, Belgium.. declercq@chim.ucl.ac.be) . Journal of molecular biology, (2001 Aug 24) 311 (4) 751-9. Journal code: 2985088R. ISSN: 0022-2836. Pub. country: England: United Kingdom. Language: English.

AB The peroxiredoxins define an emerging family of peroxidases able to reduce

hydrogen peroxide and alkyl hydroperoxides with the use of reducing equivalents derived from thiol-containing donor molecules such as thioredoxin, glutathione, trypanothione and AhpF. Peroxiredoxins have been identified in prokaryotes as well as in eukaryotes. **Peroxiredoxin 5** (**PRDX5**) is a novel type of mammalian thioredoxin peroxidase widely expressed in tissues and located cellularly to mitochondria, peroxisomes and cytosol. Functionally, **PRDX5** has been implicated in antioxidant protective mechanisms as well as in signal transduction in cells. We report here the 1.5 A resolution crystal structure of **human PRDX5** in its reduced form. The crystal structure reveals that **PRDX5** presents a thioredoxin-like domain. Interestingly, the crystal structure shows also that **PRDX5** does not form a dimer like other mammalian members of the peroxiredoxin family. In the reduced form of **PRDX5** , Cys47 and Cys151 are distant of 13.8 A although these two cysteine residues are thought to be involved in peroxide reductase activity by forming an intramolecular disulfide intermediate in the oxidized enzyme. These data suggest that the enzyme would necessitate a conformational change to form a disulfide bond between catalytic Cys47 and Cys151 upon oxidation according to proposed peroxide reduction mechanisms. Moreover, the presence of a benzoate ion, a hydroxyl radical scavenger, was noted close to the active-site pocket. The possible role of benzoate in the antioxidant activity of **PRDX5** is discussed.


L5 ANSWER 17 OF 17 MEDLINE on STN DUPLICATE 8
2001329618. PubMed ID: 11396953. Antioxidant enzyme **peroxiredoxin 5** is upregulated in degenerative **human** tendon. Wang M X; Wei A; Yuan J; Clippe A; Bernard A; Knoops B; Murrell G A. (Orthopaedic Research Institute, St. George Hospital, University of New South Wales, 4-10 South Street, Sydney, New South Wales 2217, Australia. ) Biochemical and biophysical research communications, (2001 Jun 15) 284 (3) 667-73. Journal code: 0372516. ISSN: 0006-291X. Pub. country: United States. Language: English.

AB **Peroxiredoxin 5** (**PRDX5**) is a novel thioredoxin peroxidase recently identified in a variety of **human** cells and tissues, which is considered to play an important role in oxidative stress protection mechanisms. However, little is known about its expression in tendon degeneration, a common and disabling condition that primarily affects older people, in which oxidative stress may be implicated. The present study demonstrated that normal **human** tendon expresses **PRDX5** and its expression is significantly increased in degenerative tendon. In addition, we have localized **PRDX5** to fibroblasts in normal tendon and to both fibroblasts and endothelial cells in degenerate tendon. The differential expression of **PRDX5** in normal and degenerate tendon shows that a thioredoxin peroxidase with antioxidant properties is upregulated under pathophysiological conditions and suggests that oxidative stress may be involved in the pathogenesis of tendon degeneration. **PRDX5** may play a protective role against oxidative stress during this pathophysiological process.


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L6 ANSWER 1 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
2005:182920 Document No. 142:258503 Secreted polypeptide species in human plasma, detection assays for smaller proteins and tryptic peptides, and expression profiles useful for disease diagnosis. Argoud-puy, Guilaine; Bederr, Nassima; Bougueleret, Lydie; Cusin, Isabelle; Mahe, Eve; Niknejad,

Anne; Reffas, Samia; Rose, Keith; Saudrais, Cedric; Scherer, Andreas; Papoian, Ruben; Dengler, Uwe Jochen; Croft, Laurence James (Genova Ltd., Bermuda; Novartis Ag; Novartis Pharma GmbH). PCT Int. Appl. WO 2005019825 A2 20050303, 284 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-EP9323 20040819. PRIORITY: US 2003-2003/PV496966 20030820.

AB The invention relates to polypeptide species secreted in human plasma, isolated polynucleotides encoding such polypeptides, polymorphic variants thereof, and the use of said nucleic acids and polypeptides or compns. thereof for detection assays and disease diagnosis. An industrial-scale method, involving sample pooling, is detailed for the anal. of smaller proteins (mol. weight less than about 40 kDa and mostly under 20 kDa),a nd thousands of peptides resulting from polypeptides can be identified from a single pool. Low abundance proteins such as leptin and ghrelin and peptides such as bradykinin, were clearly identified. By identifying the actual plasma polypeptide species, differences in mRNA processing and splicing, translation rate, mRNA stability, and posttranslational modifications are revealed, and plasma localization points to a novel, previously unknown function for the polypeptides of the invention. Peptides corresponding to 3 specific human plasma polypeptides (HPP) were identified and selected for functional characterization: esophageal cancer-related gene 2 (ECRG2), thymosin β4, and pancreastatin. Treatment of mice with these three HPP species resulted in gene expression profiles showing that these proteins would be useful in diagnosis treatment of cancer or hyperplasia-associated conditions, neurodegeneration or ion balance-associated diseases, and diseases associated with dysregulated serum glucose (e.g., diabetes) or metabolic disorders (e.g., amyloidosis).

L6 ANSWER 2 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

2005:572337 Document No. 143:92107 Peroxisome-associated **peroxiredoxin 5**, nucleotide sequence encoding said polypeptide and their uses in the diagnosis and/or the treatment of lung injuries and diseases, and of oxidative stress-related disorders. Knoops, Bernard; Hermans, Cedric; Bernard, Alfred; Wattiez, Ruddy; Flamagne, Paul; Plaisant, Frank; Gressens, Pierre; Murrell, George A. G.; Wang, Min-Xia (Belg.). U.S. Pat. Appl. Publ. US 2005142126 A1 20050630, 38 pp., Cont.-in-part of U.S. Ser. No. 486,167. (English). CODEN: USXXCO. APPLICATION: US 2003-686157 20031015. PRIORITY: BE 1997-692 19970820; WO 1998-BE124 19980820; US 2000-2000/486167 20000815.

AB A human peroxisome-associated polypeptide (designated **peroxiredoxin 5** or **PRDX5**) and its corresponding genomic DNA and cDNA sequence encoding the peroxisome-associated polypeptide are disclosed. Human **PRDX5** cDNA contains two ATG initiation codons, giving a long or a short **PRDX5** form; the short form contains a peroxisomal targeting signal type 1 and is localized to peroxisomes, the cytosol and the nucleus, whereas the long form has mitochondrial localization due to the presence of a mitochondrial targeting sequence which is absent in the sort form. The corresponding nucleotide and amino acid sequence from rat and mouse **PRDX5** are also provided. **PRDX5** is up-regulated by H2O2 and inflammatory cytokines for protection against oxidative stress, and plays a role in inflammatory and pneumotoxic reactions, as well as protects against excitotoxic brain lesions. The protein is useful in the diagnosis and/or treatment of several diseases, particularly lung injuries and diseases as well as oxidative stress-related disorders, particularly neurotoxic injury or excitotoxic injury.

L6 ANSWER 3 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

2005:497362 Document No. 143:42267 Genes induced in brain by exposure to β-amyloid peptides and the development of drug targets for treatment of Alzheimer's disease. Gan, Li; Gonzalez-Zulueta, Mirella; Ye, Shiming; Urfer, Roman; Nikolich, Karoly (AGY Therapeutics, Inc., USA). U.S. Pat. Appl. Publ. US 2005123962 A1 20050609, 131 pp. (English). CODEN: USXXCO. APPLICATION: US 2004-974148 20041026. PRIORITY: US 2003-2003/PV515536 20031028.

AB This invention provides a method for detecting a neurodegenerative disorder or susceptibility to a neurodegenerative disorder in a subject by identifying genes showing altered levels of expression in response to the disease. Specifically, genes induced by exposure to toxic peptides derived from β-amyloid are identified as markers for Alzheimer's disease and the gene products are identified as potential drug targets. Also included in the present invention is a method reducing toxic Aβ peptide production by a eukaryotic cell, and a method of ameliorating neurotoxicity of the peptide. The present invention further embodies compns. such as Alzheimer's Disease-associated genes, the polypeptides encoded therefrom, gene delivery vehicles, host cells and kits comprising the Alzheimer's Disease-associated genes and/or polypeptides. Genes induced by β-amyloid in hippocampus or cortex in a mouse Alzheimer's disease model were identified by subtractive hybridization. Genes induced in rat by injection of β-amyloid peptides into the hippocampus were also identified.

L6 ANSWER 4 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

2005:394682 Document No. 142:445550 Gene expression profiles for the diagnosis and prognosis of breast cancer. Erlander, Mark; Ma, Xiao-Jun; Wang, Wei; Wittliff, James L. (Arcturus Bioscience, Inc. University of Louisville, USA). U.S. Pat. Appl. Publ. US 2005095607 A1 20050505, 40 pp. (English). CODEN: USXXCO. APPLICATION: US 2004-795092 20040305. PRIORITY: US 2003-2003/PV453006 20030307.

AB The invention relates to the identification and use of gene expression profiles, or patterns, suitable for identification of breast cancer patient populations with different survival outcomes. The gene expression profiles may be embodied in nucleic acid expression, protein expression, or other expression formats, and may be used in the study and/or determination of the prognosis of a patient, including breast cancer survival.

L6 ANSWER 5 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

2005:1078815 Document No. 143:434432 Crystal structures of oxidized and reduced forms of human mitochondrial thioredoxin 2. meets, Aude; Evrard, Christine; Landtmeters, Marie; Marchand, Cecile; Knoops, Bernard; Declercq, Jean-Paul (Unit of Structural Chemistry (CSTR), Institut des Sciences de la Vie, Universite catholique de Louvain, Louvain-la-Neuve, B-1348, Belg.). Protein Science, 14(10), 2610-2621 (English) 2005. CODEN: PRCIEI. ISSN: 0961-8368. Publisher: Cold Spring Harbor Laboratory Press.

AB Mammalian thioredoxin 2 is a mitochondrial isoform of highly evolutionary conserved thioredoxins. Thioredoxins are small ubiquitous protein-disulfide oxidoreductases implicated in a large variety of biol. functions. In mammals, thioredoxin 2 is encoded by a nuclear gene and is targeted to mitochondria by a N-terminal mitochondrial presequence. Recently, mitochondrial thioredoxin 2 (TXN2) was shown to interact with components of the mitochondrial respiratory chain and to play a role in the control of mitochondrial membrane potential, regulating mitochondrial apoptosis signaling pathway. Here we report the first crystal structures of a mammalian mitochondrial thioredoxin 2. Crystal forms of reduced and oxidized human thioredoxin 2 are described at 2.0 and 1.8 Å resolution Though the folding is rather similar to that of human cytosolic/nuclear thioredoxin 1, important differences are observed during the transition between the oxidized and the reduced states of human thioredoxin 2, compared with human thioredoxin 1. In spite of the absence of the Cys residue implicated in dimer formation in human thioredoxin 1, dimerization still occurs in the crystal structure of human thioredoxin 2, mainly

mediated by hydrophobic contacts, and the dimers are associated to form two-dimensional polymers. Interestingly, the structure of human thioredoxin 2 reveals possible interaction domains with human **peroxiredoxin 5** (**PRDX5**), a substrate protein of human thioredoxin 2 in mitochondria.

L6 ANSWER 6 OF 23 MEDLINE on STN DUPLICATE 1
2005065732. PubMed ID: 15695408. Immunogenicity without immunoselection: a mutant but functional antioxidant enzyme retained in a human metastatic melanoma and targeted by CD8(+) T cells with a memory phenotype. Sensi Marialuisa; Nicolini Gabriella; Zanon Marina; Colombo Chiara; Molla Alessandra; Bersani Ilaria; Lupetti Raffaella; Parmiani Giorgio; Anichini Andrea. (Units of Immunobiology of Human Tumors, Department of Experimental Oncology, Istituto Nazionale per lo Studio e la Cura dei Tumori, Via Venezian 1, Milan, Italy.. marialuisa.sensi@istitutotumori.mi.it) . Cancer research, (2005 Jan 15) 65 (2) 632-40. Journal code: 2984705R. ISSN: 0008-5472. Pub. country: United States. Language: English.
AB Human melanomas can express unique tumor antigens, resulting from mutated proteins, and shared epitopes encoded for by normal genes, but these two classes of antigens have not been previously compared for immunogenicity and retention in metastatic cells. Here, we identified a new unique antigen generated by a point mutation in the **peroxiredoxin 5** (**Prdx5**) gene in an HLA-A*0201(+) human metastatic melanoma lacking the wild-type allele. An antioxidant assay, with recombinant **Prdx5** proteins, and evaluation of peroxide accumulation in transiently transfected cells, indicated that the mutant protein retained its enzymatic activity. The mutation in the **Prdx5** protein did not generate a new HLA agretope but yielded an HLA-A*0201-restricted T cell epitope (**Prdx5**(110-119)). By HLA-tetramer analysis, in a tumor-invaded lymph node, >50% of mutant **Prdx5**-specific CD8(+) T cells (frequency 0.37%/CD8(+)) showed a CCR7(+/-) CD45RA(-) "T(CM)" or "T(EM)" phenotype, as found in Melan-A/MART-1-specific T cells (frequency 0.68%/CD8(+)) in the same tissue. In agreement with their memory phenotype, the **Prdx5** -specific T cells readily expanded in vitro in mixed lymphocyte-tumor culture, as did the Melan-/MART-1-specific T cells. By immunohistochemistry of the invaded lymph node, the mutant **Prdx5** protein was expressed in all neoplastic cells, in contrast with the heterogeneous expression of shared antigens as Melan-A/MART-1, gp100 and tyrosinase. Thus, a unique tumor antigen can be as immunogenic as the melanoma differentiation antigens but, in contrast to the latter, may be retained in all metastatic cells possibly as result of the relevant cellular function exerted by the mutated protein.

L6 ANSWER 7 OF 23 MEDLINE on STN DUPLICATE 2
2005153168. PubMed ID: 15785239. **Peroxiredoxin 5** expression in the human thyroid gland. Gerard A-C; Many M-C; Daumerie Ch; Knoops B; Colin I M. (Unite de Morphologie Experimentale, B-1200, Bruxelles, Belgium. ) Thyroid : official journal of the American Thyroid Association, (2005 Mar) 15 (3) 205-9. Journal code: 9104317. ISSN: 1050-7256. Pub. country: United States. Language: English.
AB **Peroxiredoxin 5** (**PRDX5**) is a newly discovered thioredoxin peroxidase able to reduce peroxides that is implicated in antioxidant protective mechanisms. We report here its expression in the human thyroid gland. Twenty-seven human thyroid specimens were examined by immunohistochemistry. They included six normal thyroid tissues, five multinodular goiters, nine hot nodules, two Hurthle cell adenomas, and five thyroids from patients with Graves' disease. In the control tissue, **PRDX5** expression was heterogeneous, being stronger in cubical functionally active follicular cells than in flat quiescent thyrocytes. It was diffuse in the cytoplasm, occasionally localized in inclusions that most likely corresponded to mitochondria. This feature was particularly marked in the Hurthle cell adenoma case. In multinodular goiters, hot nodules, and Graves' thyroids, the cytosolic labeling was enhanced compared to the control tissue and a signal was also

detected in few nuclei. To determine whether the level of expression was different between multinodular goiters and hyperthyroid Graves' thyroids, **PRDX5** immunoblotting was performed in these two respective tissues. We observed that **PRDX5** expression was higher in the thyroid gland of patients with Graves' disease compared to multinodular goiters. In conclusion, our data show that **PRDX5** is expressed in the thyroid gland where it could act as antioxidant. The level of expression is directly correlated with the functional status of epithelial cells, being higher in multinodular goiters, and even more pronounced in hyperthyroid tissues, such as Graves' disease.

L6 ANSWER 8 OF 23 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
2005:519000 Document No.: PREV200510296914. Expression of peroxiredoxins in rat pancreatic beta-cells. Romanus, P. [Reprint Author]; Bol, V.; Knoops, B.; Remacle, C.; Reusens, B.. Univ Catholique Louvain, B-1348 Louvain, Belgium. Diabetologia, (2005) Vol. 48, No. Suppl. 1, pp. A185. Meeting Info.: 41st Annual Meeting of the European-Association-for-the-Study-of-Diabetes. Athens, GREECE. September 10 -15, 2005. European Assoc Study Diabet.
CODEN: DBTGAJ. ISSN: 0012-186X. Language: English.

L6 ANSWER 9 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
2004:240530 Document No. 140:419858 Crystal Structure of a Dimeric Oxidized form of Human **Peroxiredoxin 5.** Evrard, Christine; Capron, Arnaud; Marchand, Cecile; Clippe, Andre; Wattiez, Ruddy; Soumillion, Patrice; Knoops, Bernard; Declercq, Jean-Paul (Unit of Structural Chemistry (CSTR), Universite Catholique de Louvain, Louvain-la-Neuve, B-1348, Belg.). Journal of Molecular Biology, 337(5), 1079-1090 (English) 2004. CODEN: JMOBAK. ISSN: 0022-2836. Publisher: Elsevier.
AB **Peroxiredoxin 5** (**PRDX5**) is the last discovered mammalian member of an ubiquitous family of peroxidases widely distributed among prokaryotes and eukaryotes. Mammalian **peroxiredoxin 5** has been recently classified as an atypical 2-Cys peroxiredoxin due to the presence of a conserved peroxidatic N-terminal cysteine (Cys47) and an unconserved resolving C-terminal cysteine residue (Cys151) forming an intramol. disulfide intermediate in the oxidized enzyme. We have recently reported the crystal structure of human **peroxiredoxin 5** in its reduced form. Here, a new crystal form of human **peroxiredoxin 5** is described at 2.0 Å resolution The asym. unit contains three polypeptide chains. Surprisingly, beside two reduced chains, the third one is oxidized although the enzyme was crystallized under initial reducing conditions in the presence of 1 mM 1,4-dithio-DL-threitol. The oxidized polypeptide chain forms an homodimer with a symmetry-related one through intermol. disulfide bonds between Cys47 and Cys151. The formation of these disulfide bonds is accompanied by the partial unwinding of the N-terminal parts of the α2 helix, which in the reduced form contains the peroxidatic Cys47 and the α6 helix, which is sequentially close to the resolving residue Cys151. In each monomer of the oxidized chain, the C-terminal part including the α6 helix is completely reorganized and is isolated from the rest of the protein on an extended arm. In the oxidized dimer, the arm belonging to the first monomer now appears at the surface of the second subunit and vice versa.

L6 ANSWER 10 OF 23 MEDLINE on STN DUPLICATE 3
2004322097. PubMed ID: 15223323. Protection of Xenopus laevis embryos against alcohol-induced delayed gut maturation and growth retardation by **peroxiredoxin 5** and catalase. Peng Ying; Yang Pai-Hao; Ng Samuel S M; Lum Ching Tung; Kung Hsiang-Fu; Lin Marie C. (Institute of Molecular Biology and Open Lab of Chemical Biology, Institute of Molecular Technology for Drug Discovery and Synthesis, University of Hong Kong, Hong Kong, China. ) Journal of molecular biology, (2004 Jul 16) 340 (4) 819-27. Journal code: 2985088R. ISSN: 0022-2836. Pub. country: England: United Kingdom. Language: English.

AB Accumulated evidence indicates that maternal alcohol consumption causes fetal enteric damage and growth retardation. In this study, we investigated the underlying molecular mechanisms in a Xenopus model of fetal alcohol exposure. We established a condition of transient alcohol exposure that produces tadpoles with delayed gut maturation and decreased body length. We then investigated the roles of reactive oxygen species (ROS) and reactive nitrogen species (RNS) by microinjecting plasmids expressing catalase and **peroxiredoxin 5** (**PRDX5** ) into two-cell stage embryos. Finally, the effects of these enzymes on the expression of key gut developmental genes were determined by animal cap explant assay. We showed that exposure of Xenopus embryos to 0.5% alcohol from stage 13 to stage 22 produced tadpoles with delayed gut maturation, reduced growth, and down-regulation in several gut developmental genes, with VegT, Pax6 and Sox17 most vulnerable. We further demonstrated that microinjection of catalase attenuated alcohol-induced ROS production and restored the expression of VegT and Pax6, but protected the embryos from delayed gut development and retarded growth only partially. By contrast, microinjection of **PRDX5** reduced both ROS and RNS production, and prevented the gut and growth defects, and restored VegT, Pax6 and Sox17 gene expression. A positive correlation was found between delayed gut maturation and reduced body length. These results indicate the crucial roles of both the ROS-Pax6 and RNS-Sox17 signaling axes in alcohol-induced fetal gut defects and growth retardation. In addition, they suggest strongly a cause-and-effect relationship between alcohol-induced delayed gut maturation and growth retardation.

L6 ANSWER 11 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
2004:770314 Document No. 142:129690 Crystal structure of the C47S mutant of human **peroxiredoxin 5**. Evrard, Christine; Smeets, Aude; Knoops, Bernard; Declercq, Jean-Paul (Unit of Structural Chemistry, Universite catholique de Louvain, Louvain-la-Neuve, B-1348, Belg.). Journal of Chemical Crystallography, 34(8), 553-558 (English) 2004. CODEN: JCCYEV. ISSN: 1074-1542. Publisher: Springer Science+Business Media, Inc..
AB In the crystal structure of the reduced form of the wild-type human **peroxiredoxin 5** (**PRDX5**), the presence of a benzoate ion in direct interaction with the peroxidatic Cys-47 residue appeared as a rather intriguing feature since it is known that the benzoate ion can play the role of a specific hydroxyl radical scavenger. Here, the crystal structure of the C47S mutant of human **PRDX5** was crystallized in the tetragonal system, space group P41212, with a = 65.65 Å and c = 122.04 Å. It confirms the presence of this benzoate ion in spite of the mutation to Ser of the Cys-47 residue to which the benzoate ion was directly linked in the wild-type structure. The benzoate ion appeared to be stabilized by hydrophobic contacts on both sides of the aromatic ring. In this matter, the α5 helix, which was specific to **PRDX5** among mammalian PRDXs, played an important role. These hydrophobic contacts also allowed the authors to suggest why the benzoate ion disappears when the mol. is oxidized.

L6 ANSWER 12 OF 23 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 4
2004426289 EMBASE Expression of peroxiredoxins in bovine oocytes and embryos produced in vitro. Leyens G.; Knoops B.; Donnay I.. I. Donnay, U. des Sci. Veterinaires, Univ. Catholique de Louvain, Place Croix du Sud 5 bte 10, B-1348 Louvain-la-Neuve, Belgium. donnay@vete.ucl.ac.be. Molecular Reproduction and Development Vol. 69, No. 3, pp. 243-251 2004.
Refs: 54.
ISSN: 1040-452X. CODEN: MREDEE
Pub. Country: United States. Language: English. Summary Language: English.
ED Entered STN: 20041028
AB Peroxiredoxins (PRDXs) form a family of peroxidases involved in antioxidant protection and cell signaling. Due to their peroxide reductase activity, these enzymes might be involved in fine-tuning

peroxide levels in embryos during in vitro production. In this study, RT-PCR was used to examine the expression of the six PRDX isoforms (PRDX1 to PRDX6) in bovine oocytes and embryos. PRDXs were detected in oocytes both before and after in vitro maturation. Besides, PRDX6 was up-regulated after maturation. Single embryos were analyzed from the two-cell to the blastocyst stages. PRDX1 and **PRDX5** transcripts were detected throughout development. PRDX2, PRDX3, and PRDX6 were not expressed around the 9- to 16-cell stage. PRDX4 transcripts were weakly detected in pools of embryos from the 9- to 16-cell stage onwards. In situ immunodetection of **PRDX5**, which was previously reported to exhibit the widest subcellular distribution among PRDXs in adult mammalian cells, showed a mitochondrial distribution pattern in the bovine embryo. Finally, the potential modulation by oxidative stress of PRDX expression around the major embryonic genome activation was evaluated by culturing embryos under 20% O(2) instead of 5%. No significant difference in the pattern of PRDX expression was observed under 20% O (2). In conclusion, our data show for the first time that PRDXs are expressed in mammalian oocytes and early embryos. Moreover, the bovine transcripts exhibit various patterns of expression that might be related to the potential role of PRDXs in oocyte maturation and embryo development. .COPYRGT. 2004 Wiley-Liss, Inc.

L6 ANSWER 13 OF 23 MEDLINE on STN DUPLICATE 5

2004372414. PubMed ID: 15276323. Overexpression of antioxidant enzyme **peroxiredoxin 5** protects human tendon cells against apoptosis and loss of cellular function during oxidative stress. Yuan Jun; Murrell George A C; Trickett Annette; Landtmeters Marie; Knoops Bernard; Wang Min-Xia. (Orthopaedic Research Institute, St. George Hospital Campus, 4-10 South Street, University of New South Wales, Sydney, NSW 2217, Australia. ) Biochimica et biophysica acta, (2004 Jul 23) 1693 (1) 37-45. Journal code: 0217513. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.

AB Oxidative stress and apoptosis are implicated in tendon degeneration. **Peroxiredoxin 5** (**PRDX5**) is a novel thioredoxin peroxidase recently identified in mammals, participating directly in eliminating hydrogen peroxide (H(2)O(2)) and neutralizing other reactive oxygen species (ROS). We have previously reported that **PRDX5** is upregulated in degenerative human tendon. However, the effects of this upregulation on human tendon cell function remain unknown, in particular, with regards to oxidative stress conditions. Here we report that exposure of human tendon cells to 50 microM H(2)O(2) for 24 h (in vitro oxidative stress) caused a significant increase in the percentage of apoptotic cells ($P<0.05$) as assessed by flow cytometric analysis of Annexin V binding, accompanied by increased PRXD5 mRNA and protein expression. Overexpression of **PRDX5** in human tendon cells via transfection inhibited H(2)O(2)-induced tendon cell apoptosis by 46% ($P<0.05$), and prevented the decrease in tendon cell collagen synthesis which occurs under H(2)O(2) challenge, although the decrease in collagen synthesis was small. Results from our study indicate that the antioxidant enzyme **PRDX5** plays a protective role in human tendon cells against oxidative stress by reducing apoptosis and maintaining collagen synthesis.

L6 ANSWER 14 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

2003:967377 Document No. 140:230218 Cloning of bovine peroxiredoxins-gene expression in bovine tissues and amino acid sequence comparison with rat, mouse and primate peroxiredoxins. Leyens, Gregory; Donnay, Isabelle; Knoops, Bernard (Institut des Sciences de la Vie, Unite des Sciences Veterinaires, Universite Catholique de Louvain, Louvain-la-Neuve, B-1348, Belg.). Comparative Biochemistry and Physiology, Part B: Biochemistry & Molecular Biology, 136B(4), 943-955 (English) 2003. CODEN: CBPBB8. ISSN: 1096-4959. Publisher: Elsevier.

AB The peroxiredoxin (PRDX) family is a recently identified family of peroxidases found in organisms ranging from bacteria to mammals. In mammals, six PRDX isoforms have been characterized in human (Homo sapiens), rat (Rattus norvegicus) and mouse (Mus musculus). PRDXs are

cytosolic, secreted or targeted to organelles such as peroxisomes, mitochondria and the nucleus. Some PRDXs are synthesized as larger precursor proteins with a presequence that is cleaved to produce the mature form. To study the expression of the six PRDXs in bovine (Bos taurus), we first cloned cDNAs coding for PRDX1, PRDX2, PRDX4 and **PRDX5.** PRDX3 and PRDX6 had previously been cloned and characterized in bovine. The comparison of bovine PRDXs with their rat, mouse and primate orthologues reveals a min. of 95% similarity of mature proteins. Even though mitochondrial or export signal presequences are normally less conserved, the unprocessed proteins still present a min. of 84% similarity. Nevertheless, a major divergence lies at the N-terminus of bovine PRDX2, where a Cys-Val-Cys motif was identified. The expression of the six PRDXs in 22 bovine tissues has been studied by RT-PCR. Our results point out the ubiquity of the different PRDX transcripts in bovine tissues. The important conservation of the different PRDXs, the multiple processes they have been associated with, as well as the ubiquity of all the members of the family analyzed in this study for the first time altogether, suggest that they play a major role in the basal metabolism of mammalian cells.

L6 ANSWER 15 OF 23 MEDLINE on STN DUPLICATE 6
2003148414. PubMed ID: 12654475. Recombinant **peroxiredoxin 5** protects against excitotoxic brain lesions in newborn mice. Plaisant Frank; Clippe Andre; Vander Stricht Delphine; Knoops Bernard; Gressens Pierre. (INSERM E 9935 and Service de Neurologie Pediatrique, Hopital Robert-Debre, Paris, France. ) Free radical biology & medicine, (2003 Apr 1) 34 (7) 862-72. Journal code: 8709159. ISSN: 0891-5849. Pub. country: United States. Language: English.

AB The pathophysiology of brain lesions associated with cerebral palsy is multifactorial and likely involves excess release of glutamate and excess production of free radicals, among other factors. Theoretically, antioxidants could limit the severity of these brain lesions. Peroxiredoxins are a family of peroxidases widely distributed in eukaryotes and prokaryotes. **Peroxiredoxin 5** ( **PRDX5**) is a recently discovered mammalian member of this family of antioxidant enzymes that is able to reduce hydrogen peroxide and alkyl hydroperoxides. The present study was designed to examine the neuroprotective effects of recombinant **PRDX5** against neonatal excitotoxic challenge in both in vivo and in vitro experiments. For in vivo experiments, mice (postnatal day 5) were injected intraneopallially with ibotenate acting on NMDA and metabotropic receptors, or S-bromowillardiine acting on AMPA-kainate receptors to produce excitotoxic stress and brain lesions. Systemically administered recombinant **PRDX5** provided protection against ibotenate-induced excitotoxic stress. Brain lesions of animals given ibotenate and **PRDX5** were up to 63% smaller than that given ibotenate alone. However, **PRDX5** provided no prevention from lesions induced with S-bromowillardiine. A mutated recombinant **PRDX5** that is devoid of peroxidase activity was also tested and showed no protection against lesions induced by either ibotenate or S-bromowillardiine. Two classical antioxidants, N-acetylcysteine and catalase-PEG, provided the same neuroprotective effect as **PRDX5.** For in vitro experiments, neocortical neurons were exposed to 300 microM NMDA alone, NMDA plus recombinant **PRDX5** , or NMDA, recombinant **PRDX5** and dithiothreitol, a classical electron donor for peroxiredoxins. Recombinant **PRDX5** plus dithiothreitol displayed a synergistic neuroprotective effect on NMDA-induced neuronal death. These findings indicate that reactive oxygen species production participates in the formation of NMDA receptor-mediated brain lesions in newborn mice and that antioxidant compounds, such as **PRDX5**, provide some neuroprotection in these models.

L6 ANSWER 16 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
2002:594988 Document No. 137:151800 Crystal structure of **peroxiredoxin 5** and its use for design of structural homologues for treating oxidative-stress related disorders. Declercq,

Jean-Paul; Knoops, Bernard; Evrard, Christine; Clippe, Andre; Van der Stricht, Delphine; Bernard, Alfred (Universite Catholique De Louvain, Belg.). PCT Int. Appl. WO 2002061063 A1 20020808, 101 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-EP890 20020129. PRIORITY: EP 2001-870016 20010130.

AB The present invention provides the crystal structure of **peroxiredoxin 5** (**PRDX5**), which allows to determine the key structural features of active binding pocket of **PRDX5**. The present invention relates to a crystal comprising a **PRDX5** protein in crystalline form that has the tetragonal space group symmetry P41 21 2. The invention further relates to a method for synthesizing a homolog of said crystal or an active binding site pocket , wherein said method comprises (a) providing the coordinates of the active binding site pocket of **PRDX5**, defined by residues of Table 2 and structure coordinates in Table 1, to a computer modeling system, (b) designing a homolog of said crystal or said active binding site pocket; (c) synthesizing said homolog, (d) optionally screening said homolog in a peroxidase activity assay for determining its catalytic activity, and (e) if desired, determining whether said compound inhibits oxidation in an antioxidant activity assay.

L6 ANSWER 17 OF 23 MEDLINE on STN DUPLICATE 7

2002660121. PubMed ID: 12420131. Confirmation and high resolution mapping of an atherosclerosis susceptibility gene in mice on Chromosome 1. Phelan Shelley A; Beier David R; Higgins David C; Paigen Beverly. (Biology Department, Fairfield University, North Benson Road, Fairfield, Connecticut 06430, USA.. sphelan@fair1.fairfield.edu) . Mammalian genome : official journal of the International Mammalian Genome Society, (2002 Oct) 13 (10) 548-53. Journal code: 9100916. ISSN: 0938-8990. Pub. country: United States. Language: English.

AB Previously, we demonstrated that Ath1 is a quantitative trait locus for aortic fatty streak formation, located on Chromosome (chr) 1, with susceptibility in C57BL/6J mice and resistance in C3H/HeJ and BALB/cJ mice fed an atherogenic diet. In this study, we find an atherosclerosis susceptibility locus in the same region of Chr 1 by constructing two congenic strains with the resistance phenotype transferred from different resistant strains, PERA/EiJ or SPRETUS/EiJ. By backcrossing one congenic strain to C57BL/6J and testing recombinant animals, we reduced the distance of the atherosclerosis susceptibility region to 2.3 cM between D1Mit14 and D1Mit10. Further testing of nine recombinant animals showed that eight of the nine were consistent with a further narrowing between D1Mit159 and D1Mit398 a distance of 0.66 cM. This region encompasses a number of potential candidate genes including the thiol-specific antioxidant gene Aop2, also known as **peroxiredoxin 5** ( **Prdx5**). AOP2 is capable of reducing hydroperoxides and lipid peroxides in the cell. To investigate Aop2 as a potential candidate, we mapped Aop2 in our backcross and localized it to the atherosclerosis susceptibility interval. We determined that Aop2 is highly expressed in atherosclerosis-related tissues including liver and heart. We also found an inverse correlation between Aop2 mRNA in liver and atherosclerosis phenotype for strains C57BL/6 and the resistant congenic derived from SPRETUS/EiJ. Since LDL oxidation has been implicated in the pathogenesis of this disease, and AOP2 possesses antioxidant activity, we suggest the role of Aop2 in atherosclerosis susceptibility needs to be further explored.

L6 ANSWER 18 OF 23 MEDLINE on STN DUPLICATE 8

2003015431. PubMed ID: 12522579. Identification of calcium-induced genes

in HaCaT keratinocytes by polymerase chain reaction-based subtractive hybridization. Seo Eun-Young; Piao Yong-Jun; Kim Jeong-Soo; Suhr Ki-Beom; Park Jang-Kyu; Lee Jeung-Hoon. (Department of Dermatology, Chungnam University Hospital, Daesa-dong 640, Jung-gu, Daejeon 301-040, South Korea. ) Archives of dermatological research, (2002 Dec) 294 (9) 411-8. Electronic Publication: 2002-11-05. Journal code: 8000462. ISSN: 0340-3696. Pub. country: Germany: Germany, Federal Republic of. Language: English.

AB Suppression subtractive hybridization, a PCR-based method for cDNA subtraction, was used to identify differentially expressed genes in keratinocytes. Differentiation was induced by elevating the calcium level in the cell culture medium. Using HaCaT immortalized keratinocytes cultured in the presence of a high calcium concentration, we isolated 60 clones representing 48 different genes. By reverse Northern analysis, 13 genes were scored as overexpressed in these HaCaT cells. Northern blot analysis was used to confirm differential gene expression. Six genes, keratin 1, plasminogen activator inhibitor type 2 (PAI-2), ferritin H, **peroxiredoxin 5** (**PRDX5**), insulin-like growth factor binding protein-3 (IGFBP-3), and one EST gene, were differentially expressed in HaCaT cells cultured in the presence of a high calcium concentration. Two of these genes, keratin 1 and PAI-2, are differentially expressed during keratinocyte terminal differentiation. IGFBP-3, which has reduced expression during epidermal differentiation, was increased after culture in a high-calcium medium for 2 or 5 days. Overexpression of the ferritin H and **PRDX5** genes due to elevated calcium has not been reported in keratinocytes. We demonstrated the expression of IGFBP-3, ferritin H, **PRDX5**, and one gene of a matching sequence from the EST database during differentiation in primary cultured normal human keratinocytes. The EST gene expressed two transcripts of 1.8 kb and 2.5 kb in HaCaT cells, and the transcripts were confirmed to increase in keratinocytes cultured in a high-calcium medium.

L6 ANSWER 19 OF 23 MEDLINE on STN DUPLICATE 9

2002657506. PubMed ID: 12417342. Expression and regulation of **peroxiredoxin 5** in human osteoarthritis. Wang Min Xia; Wei Aiqun; Yuan Jun; Trickett Annette; Knoops Bernard; Murrell George A C. (Orthopaedic Research Institute, St George Hospital, University of New South Wales, Sydney, NSW, Australia. ) FEBS letters, (2002 Nov 6) 531 (2) 359-62. Journal code: 0155157. ISSN: 0014-5793. Pub. country: Netherlands. Language: English.

AB Reactive oxygen species (ROS) are implicated in the pathogenesis of osteoarthritis (OA). However, little is known about the antioxidant defence system in articular cartilage. We investigated the expression and regulation of **peroxiredoxin 5** (**PRDX5**), a newly discovered thioredoxin peroxidase, in human normal and osteoarthritic cartilage. Our results show that human cartilage constitutively expresses **PRDX5.** Moreover, the expression is up-regulated in OA. Inflammatory cytokines tumour necrosis factor alpha and interleukin 1 beta contribute to this up-regulation by increasing intracellular ROS production. The present study suggests that **PRDX5** may play a protective role against oxidative stress in human cartilage.

L6 ANSWER 20 OF 23 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

2003:326944 Document No.: PREV200300326944. ANTIOXIDANT ENZYME **PEROXIREDOXIN 5** IS EXPRESSED AT LOWER LEVELS IN NEURONS VULNERABLE TO CELL DEATH IN ALZHEIMER'S DISEASE. Landtmeters, M. [Reprint Author]; Alzate, L. [Reprint Author]; Brion, J. P.; Knoops, B. [Reprint Author]. Laboratory of Cell Biology, Universit Catholique de Louvain, Louvain-la-Neuve, Belgium. Society for Neuroscience Abstract Viewer and Itinerary Planner, (2002) Vol. 2002, pp. Abstract No. 784.4. http://sfn.scholarone.com. cd-rom.
Meeting Info.: 32nd Annual Meeting of the Society for Neuroscience. Orlando, Florida, USA. November 02-07, 2002. Society for Neuroscience.

Language: English.

AB **Peroxiredoxin 5** (**PRDX5**) is a peroxidase of the mitochondrial thioredoxin system which is thought to play a major protective role against oxidative damages. Many neurological disorders, including Alzheimers disease (AD), are associated with oxidative stress and mitochondria have been implicated in such a process. In AD, the hippocampus is one of the first region of the brain to develop neuropathological lesions and is, in advanced cases, an heavily affected area. To determine whether the vulnerability of certain neuronal populations of the hippocampus could be due to a less efficient protection by the mitochondrial thioredoxin system, we analyzed by immunohistochemistry the expression of **PRDX5** in the hippocampus of adults rats, of normal control humans and of AD patients. Our results show that **PRDX5** is well expressed in neurons of CA4 and CA2/3 sectors, and of the subiculum. However, **PRDX5** immunoreactivity was weak in neurons of the CA1 sector and of the dentate gyrus. In AD brains, **PRDX5** expression in CA1 decreased or was totally absent. Moreover, we tested in COS-7 cells the protection conferred by **PRDX5** overexpression against oxidative stress induced by peroxides. At 100 M tert-butyl hydroperoxide, high expression of **PRDX5** decreased significantly apoptotic cell death. These results suggest that high levels of **PRDX5** may play an important protective role against oxidative stress. We conclude that the vulnerability of certain neuronal populations of the hippocampus in AD could be partly due to a weak expression of **PRDX5.**

L6 ANSWER 21 OF 23 MEDLINE on STN DUPLICATE 10

2001475436. PubMed ID: 11518528. Crystal structure of human **peroxiredoxin 5**, a novel type of mammalian peroxiredoxin at 1.5 A resolution. Declercq J P; Evrard C; Clippe A; Stricht D V; Bernard A; Knoops B. (Universite Catholique de Louvain, Unit of Structural Chemistry (CSTR), 1 place Louis Pasteur, Louvain-la-Neuve, B-1348, Belgium.. declercq@chim.ucl.ac.be) . Journal of molecular biology, (2001 Aug 24) 311 (4) 751-9. Journal code: 2985088R. ISSN: 0022-2836. Pub. country: England: United Kingdom. Language: English.

AB The peroxiredoxins define an emerging family of peroxidases able to reduce hydrogen peroxide and alkyl hydroperoxides with the use of reducing equivalents derived from thiol-containing donor molecules such as thioredoxin, glutathione, trypanothione and AhpF. Peroxiredoxins have been identified in prokaryotes as well as in eukaryotes. **Peroxiredoxin 5** (**PRDX5**) is a novel type of mammalian thioredoxin peroxidase widely expressed in tissues and located cellularly to mitochondria, peroxisomes and cytosol. Functionally, **PRDX5** has been implicated in antioxidant protective mechanisms as well as in signal transduction in cells. We report here the 1.5 A resolution crystal structure of human **PRDX5** in its reduced form. The crystal structure reveals that **PRDX5** presents a thioredoxin-like domain. Interestingly, the crystal structure shows also that **PRDX5** does not form a dimer like other mammalian members of the peroxiredoxin family. In the reduced form of **PRDX5**, Cys47 and Cys151 are distant of 13.8 A although these two cysteine residues are thought to be involved in peroxide reductase activity by forming an intramolecular disulfide intermediate in the oxidized enzyme. These data suggest that the enzyme would necessitate a conformational change to form a disulfide bond between catalytic Cys47 and Cys151 upon oxidation according to proposed peroxide reduction mechanisms. Moreover, the presence of a benzoate ion, a hydroxyl radical scavenger, was noted close to the active-site pocket. The possible role of benzoate in the antioxidant activity of **PRDX5** is discussed.


L6 ANSWER 22 OF 23 MEDLINE on STN DUPLICATE 11

2001329618. PubMed ID: 11396953. Antioxidant enzyme **peroxiredoxin 5** is upregulated in degenerative human tendon. Wang M X; Wei A; Yuan J; Clippe A; Bernard A; Knoops B; Murrell G A. (Orthopaedic Research

Institute, St. George Hospital, University of New South Wales, 4-10 South Street, Sydney, New South Wales 2217, Australia. ) Biochemical and biophysical research communications, (2001 Jun 15) 284 (3) 667-73. Journal code: 0372516. ISSN: 0006-291X. Pub. country: United States. Language: English.

AB **Peroxiredoxin 5** (**PRDX5**) is a novel thioredoxin peroxidase recently identified in a variety of human cells and tissues, which is considered to play an important role in oxidative stress protection mechanisms. However, little is known about its expression in tendon degeneration, a common and disabling condition that primarily affects older people, in which oxidative stress may be implicated. The present study demonstrated that normal human tendon expresses **PRDX5** and its expression is significantly increased in degenerative tendon. In addition, we have localized **PRDX5** to fibroblasts in normal tendon and to both fibroblasts and endothelial cells in degenerate tendon. The differential expression of **PRDX5** in normal and degenerate tendon shows that a thioredoxin peroxidase with antioxidant properties is upregulated under pathophysiological conditions and suggests that oxidative stress may be involved in the pathogenesis of tendon degeneration. **PRDX5** may play a protective role against oxidative stress during this pathophysiological process. Copyright 2001 Academic Press.

L6 ANSWER 23 OF 23 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

1999:497298 Document No.: PREV199900497298. Genetic mapping of six mouse peroxiredoxin genes and fourteen peroxiredoxin related sequences. Lyu, Myung S.; Rhee, Sue Goo; Chae, Ho Zoon; Lee, Tae Hoon; Adamson, M. Charlene; Kang, Sang Won; Jin, Dong-Yan; Jeang, Kuan-Teh; Kozak, Christine A. [Reprint author]. Laboratory of Molecular Microbiology, National Institute of Allergy and Infectious Diseases, NIH, 4 Center Drive MSC 0460, Building 4, Room 329, Bethesda, MD, 20892-0460, USA. Mammalian Genome, (Oct., 1999) Vol. 10, No. 10, pp. 1017-1019. print. CODEN: MAMGEC. ISSN: 0938-8990. Language: English.

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                OR FLAMAGNE P?/AU OR PLAISANT F?/AU OR GRESSENS P?/AU OR MURREL
              L G?/AU OR WANG M?/AU)

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L9 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

2005:572337 Document No. 143:92107 Peroxisome-associated peroxiredoxin 5, nucleotide sequence encoding said polypeptide and their uses in the diagnosis and/or the treatment of lung injuries and diseases, and of oxidative stress-related disorders. **Knoops, Bernard**; **Hermans, Cedric**; **Bernard, Alfred**; **Wattiez, Ruddy** ; **Flamagne, Paul**; **Plaisant, Frank**; **Gressens, Pierre**; **Murrell, George A. G.**; **Wang, Min-Xia** (Belg.). U.S. Pat. Appl. Publ. US 2005142126 A1 20050630, 38 pp., Cont.-in-part of U.S. Ser. No. 486,167. (English). CODEN: USXXCO. APPLICATION: US 2003-686157 20031015. PRIORITY: BE 1997-692 19970820; WO 1998-BE124 19980820; US 2000-2000/486167 20000815.

AB A human peroxisome-associated polypeptide (designated peroxiredoxin 5 or **PRDX5**) and its corresponding genomic DNA and cDNA sequence

encoding the peroxisome-associated polypeptide are disclosed. Human **PRDX5** cDNA contains two ATG initiation codons, giving a long or a short **PRDX5** form; the short form contains a peroxisomal targeting signal type 1 and is localized to peroxisomes, the cytosol and the nucleus, whereas the long form has mitochondrial localization due to the presence of a mitochondrial targeting sequence which is absent in the sort form. The corresponding nucleotide and amino acid sequence from rat and mouse **PRDX5** are also provided. **PRDX5** is up-regulated by H2O2 and inflammatory cytokines for protection against oxidative stress, and plays a role in inflammatory and pneumotoxic reactions, as well as protects against excitotoxic brain lesions. The protein is useful in the diagnosis and/or treatment of several diseases, particularly lung injuries and diseases as well as oxidative stress-related disorders, particularly neurotoxic injury or excitotoxic injury.

L9 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
2005:1078815 Document No. 143:434432 Crystal structures of oxidized and reduced forms of human mitochondrial thioredoxin 2. meets, Aude; Evrard, Christine; Landtmeters, Marie; Marchand, Cecile; **Knoops, Bernard** ; Declercq, Jean-Paul (Unit of Structural Chemistry (CSTR), Institut des Sciences de la Vie, Universite catholique de Louvain, Louvain-la-Neuve, B-1348, Belg.). Protein Science, 14(10), 2610-2621 (English) 2005. CODEN: PRCIEI. ISSN: 0961-8368. Publisher: Cold Spring Harbor Laboratory Press.

AB Mammalian thioredoxin 2 is a mitochondrial isoform of highly evolutionary conserved thioredoxins. Thioredoxins are small ubiquitous protein-disulfide oxidoreductases implicated in a large variety of biol. functions. In mammals, thioredoxin 2 is encoded by a nuclear gene and is targeted to mitochondria by a N-terminal mitochondrial presequence. Recently, mitochondrial thioredoxin 2 (TXN2) was shown to interact with components of the mitochondrial respiratory chain and to play a role in the control of mitochondrial membrane potential, regulating mitochondrial apoptosis signaling pathway. Here we report the first crystal structures of a mammalian mitochondrial thioredoxin 2. Crystal forms of reduced and oxidized human thioredoxin 2 are described at 2.0 and 1.8 Å resolution Though the folding is rather similar to that of human cytosolic/nuclear thioredoxin 1, important differences are observed during the transition between the oxidized and the reduced states of human thioredoxin 2, compared with human thioredoxin 1. In spite of the absence of the Cys residue implicated in dimer formation in human thioredoxin 1, dimerization still occurs in the crystal structure of human thioredoxin 2, mainly mediated by hydrophobic contacts, and the dimers are associated to form two-dimensional polymers. Interestingly, the structure of human thioredoxin 2 reveals possible interaction domains with human peroxiredoxin 5 (**PRDX5**), a substrate protein of human thioredoxin 2 in mitochondria.

L9 ANSWER 3 OF 15 MEDLINE on STN DUPLICATE 1
2005153168. PubMed ID: 15785239. Peroxiredoxin 5 expression in the human thyroid gland. Gerard A-C; Many M-C; Daumerie Ch; **Knoops B**; Colin I M. (Unite de Morphologie Experimentale, B-1200, Bruxelles, Belgium. ) Thyroid : official journal of the American Thyroid Association, (2005 Mar) 15 (3) 205-9. Journal code: 9104317. ISSN: 1050-7256. Pub. country: United States. Language: English.

AB Peroxiredoxin 5 (**PRDX5**) is a newly discovered thioredoxin peroxidase able to reduce peroxides that is implicated in antioxidant protective mechanisms. We report here its expression in the human thyroid gland. Twenty-seven human thyroid specimens were examined by immunohistochemistry. They included six normal thyroid tissues, five multinodular goiters, nine hot nodules, two Hurthle cell adenomas, and five thyroids from patients with Graves' disease. In the control tissue, **PRDX5** expression was heterogeneous, being stronger in cubical functionally active follicular cells than in flat quiescent thyrocytes. It was diffuse in the cytoplasm, occasionally localized in inclusions that

most likely corresponded to mitochondria. This feature was particularly marked in the Hurthle cell adenoma case. In multinodular goiters, hot nodules, and Graves' thyroids, the cytosolic labeling was enhanced compared to the control tissue and a signal was also detected in few nuclei. To determine whether the level of expression was different between multinodular goiters and hyperthyroid Graves' thyroids, **PRDX5** immunoblotting was performed in these two respective tissues. We observed that **PRDX5** expression was higher in the thyroid gland of patients with Graves' disease compared to multinodular goiters. In conclusion, our data show that **PRDX5** is expressed in the thyroid gland where it could act as antioxidant. The level of expression is directly correlated with the functional status of epithelial cells, being higher in multinodular goiters, and even more pronounced in hyperthyroid tissues, such as Graves' disease.

L9 ANSWER 4 OF 15 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
2005:519000 Document No.: PREV200510296914. Expression of peroxiredoxins in rat pancreatic beta-cells. Romanus, P. [Reprint Author]; Bol, V.; **Knoops, B.**; Remacle, C.; Reusens, B.. Univ Catholique Louvain, B-1348 Louvain, Belgium. Diabetologia, (2005) Vol. 48, No. Suppl. 1, pp. A185.
Meeting Info.: 41st Annual Meeting of the European-Association-for-the-Study-of-Diabetes. Athens, GREECE. September 10 -15, 2005. European Assoc Study Diabet.
CODEN: DBTGAJ. ISSN: 0012-186X. Language: English.

L9 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
2004:240530 Document No. 140:419858 Crystal Structure of a Dimeric Oxidized form of Human Peroxiredoxin 5. Evrard, Christine; Capron, Arnaud; Marchand, Cecile; Clippe, Andre; **Wattiez, Ruddy**; Soumillion, Patrice; **Knoops, Bernard**; Declercq, Jean-Paul (Unit of Structural Chemistry (CSTR), Universite Catholique de Louvain, Louvain-la-Neuve, B-1348, Belg.). Journal of Molecular Biology, 337(5), 1079-1090 (English) 2004. CODEN: JMOBAK. ISSN: 0022-2836. Publisher: Elsevier.
AB Peroxiredoxin 5 (**PRDX5**) is the last discovered mammalian member of an ubiquitous family of peroxidases widely distributed among prokaryotes and eukaryotes. Mammalian peroxiredoxin 5 has been recently classified as an atypical 2-Cys peroxiredoxin due to the presence of a conserved peroxidatic N-terminal cysteine (Cys47) and an unconserved resolving C-terminal cysteine residue (Cys151) forming an intramol. disulfide intermediate in the oxidized enzyme. We have recently reported the crystal structure of human peroxiredoxin 5 in its reduced form. Here, a new crystal form of human peroxiredoxin 5 is described at 2.0 Å resolution The asym. unit contains three polypeptide chains. Surprisingly, beside two reduced chains, the third one is oxidized although the enzyme was crystallized under initial reducing conditions in the presence of 1 mM 1,4-dithio-DL-threitol. The oxidized polypeptide chain forms an homodimer with a symmetry-related one through intermol. disulfide bonds between Cys47 and Cys151. The formation of these disulfide bonds is accompanied by the partial unwinding of the N-terminal parts of the α2 helix, which in the reduced form contains the peroxidatic Cys47 and the α6 helix, which is sequentially close to the resolving residue Cys151. In each monomer of the oxidized chain, the C-terminal part including the α6 helix is completely reorganized and is isolated from the rest of the protein on an extended arm. In the oxidized dimer, the arm belonging to the first monomer now appears at the surface of the second subunit and vice versa.

L9 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
2004:770314 Document No. 142:129690 Crystal structure of the C47S mutant of human peroxiredoxin 5. Evrard, Christine; Smeets, Aude; **Knoops, Bernard**; Declercq, Jean-Paul (Unit of Structural Chemistry, Universite catholique de Louvain, Louvain-la-Neuve, B-1348, Belg.). Journal of Chemical Crystallography, 34(8), 553-558 (English) 2004.

CODEN: JCCYEV. ISSN: 1074-1542. Publisher: Springer Science+Business Media, Inc..

AB In the crystal structure of the reduced form of the wild-type human peroxiredoxin 5 (**PRDX5**), the presence of a benzoate ion in direct interaction with the peroxidatic Cys-47 residue appeared as a rather intriguing feature since it is known that the benzoate ion can play the role of a specific hydroxyl radical scavenger. Here, the crystal structure of the C47S mutant of human **PRDX5** was crystallized in the tetragonal system, space group P41212, with a = 65.65 Å and c = 122.04 Å. It confirms the presence of this benzoate ion in spite of the mutation to Ser of the Cys-47 residue to which the benzoate ion was directly linked in the wild-type structure. The benzoate ion appeared to be stabilized by hydrophobic contacts on both sides of the aromatic ring. In this matter, the α5 helix, which was specific to **PRDX5** among mammalian PRDXs, played an important role. These hydrophobic contacts also allowed the authors to suggest why the benzoate ion disappears when the mol. is oxidized.

L9 ANSWER 7 OF 15 MEDLINE on STN DUPLICATE 2

2004442317. PubMed ID: 15349835. Expression of peroxiredoxins in bovine oocytes and embryos produced in vitro. Leyens Gregory; **Knoops Bernard**; Donnay Isabelle. (Veterinary Unit, Institut des Sciences de la Vie, Universite Catholique de Louvain, Place Croix du Sud 5, Louvain-la-Neuve, Belgium. ) Molecular reproduction and development, (2004 Nov) 69 (3) 243-51. Journal code: 8903333. ISSN: 1040-452X. Pub. country: United States. Language: English.

AB Peroxiredoxins (PRDXs) form a family of peroxidases involved in antioxidant protection and cell signaling. Due to their peroxide reductase activity, these enzymes might be involved in fine-tuning peroxide levels in embryos during in vitro production. In this study, RT-PCR was used to examine the expression of the six PRDX isoforms (PRDX1 to PRDX6) in bovine oocytes and embryos. PRDXs were detected in oocytes both before and after in vitro maturation. Besides, PRDX6 was up-regulated after maturation. Single embryos were analyzed from the two-cell to the blastocyst stages. PRDX1 and **PRDX5** transcripts were detected throughout development. PRDX2, PRDX3, and PRDX6 were not expressed around the 9- to 16-cell stage. PRDX4 transcripts were weakly detected in pools of embryos from the 9- to 16-cell stage onwards. In situ immunodetection of **PRDX5**, which was previously reported to exhibit the widest subcellular distribution among PRDXs in adult mammalian cells, showed a mitochondrial distribution pattern in the bovine embryo. Finally, the potential modulation by oxidative stress of PRDX expression around the major embryonic genome activation was evaluated by culturing embryos under 20% O2 instead of 5%. No significant difference in the pattern of PRDX expression was observed under 20% O2. In conclusion, our data show for the first time that PRDXs are expressed in mammalian oocytes and early embryos. Moreover, the bovine transcripts exhibit various patterns of expression that might be related to the potential role of PRDXs in oocyte maturation and embryo development.

L9 ANSWER 8 OF 15 MEDLINE on STN DUPLICATE 3

2004372414. PubMed ID: 15276323. Overexpression of antioxidant enzyme peroxiredoxin 5 protects human tendon cells against apoptosis and loss of cellular function during oxidative stress. Yuan Jun; **Murrell George A C**; Trickett Annette; Landtmeters Marie; **Knoops Bernard**; **Wang Min-Xia.** (Orthopaedic Research Institute, St. George Hospital Campus, 4-10 South Street, University of New South Wales, Sydney, NSW 2217, Australia. ) Biochimica et biophysica acta, (2004 Jul 23) 1693 (1) 37-45. Journal code: 0217513. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.

AB Oxidative stress and apoptosis are implicated in tendon degeneration. Peroxiredoxin 5 (**PRDX5**) is a novel thioredoxin peroxidase recently identified in mammals, participating directly in eliminating hydrogen peroxide (H(2)O(2)) and neutralizing other reactive oxygen species (ROS). We have previously reported that **PRDX5** is

upregulated in degenerative human tendon. However, the effects of this upregulation on human tendon cell function remain unknown, in particular, with regards to oxidative stress conditions. Here we report that exposure of human tendon cells to 50 microM H(2)O(2) for 24 h (in vitro oxidative stress) caused a significant increase in the percentage of apoptotic cells ($P<0.05$) as assessed by flow cytometric analysis of Annexin V binding, accompanied by increased PRXD5 mRNA and protein expression. Overexpression of **PRDX5** in human tendon cells via transfection inhibited H(2)O(2)-induced tendon cell apoptosis by 46% ($P<0.05$), and prevented the decrease in tendon cell collagen synthesis which occurs under H(2)O(2) challenge, although the decrease in collagen synthesis was small. Results from our study indicate that the antioxidant enzyme **PRDX5** plays a protective role in human tendon cells against oxidative stress by reducing apoptosis and maintaining collagen synthesis.

L9 ANSWER 9 OF 15 MEDLINE on STN DUPLICATE 4

2003581906. PubMed ID: 14662316. Cloning of bovine peroxiredoxins-gene expression in bovine tissues and amino acid sequence comparison with rat, mouse and primate peroxiredoxins. Leyens Gregory; Donnay Isabelle; **Knoops Bernard.** (Unite des Sciences veterinaires, Institut des Sciences de la Vie, Universite catholique de Louvain, Place Croix du Sud 5, B-1348 Louvain-la-Neuve, Belgium.. leyens@vete.ucl.ac.be) . Comparative biochemistry and physiology. Part B, Biochemistry & molecular biology, (2003 Dec) 136 (4) 943-55. Journal code: 9516061. ISSN: 1096-4959. Pub. country: England: United Kingdom. Language: English.

AB The peroxiredoxin (PRDX) family is a recently identified family of peroxidases found in organisms ranging from bacteria to mammals. In mammals, six PRDX isoforms have been characterized in human (Homo sapiens), rat (Rattus norvegicus) and mouse (Mus musculus). PRDXs are cytosolic, secreted or targeted to organelles such as peroxisomes, mitochondria and the nucleus. Some PRDXs are synthesized as larger precursor proteins with a presequence that is cleaved to produce the mature form. To study the expression of the six PRDXs in bovine (Bos taurus), we first cloned cDNAs coding for PRDX1, PRDX2, PRDX4 and **PRDX5.** PRDX3 and PRDX6 had previously been cloned and characterized in bovine. The comparison of bovine PRDXs with their rat, mouse and primate orthologues reveals a minimum of 95% similarity of mature proteins. Even though mitochondrial or export signal presequences are normally less conserved, the unprocessed proteins still present a minimum of 84% similarity. Nevertheless, a major divergence lies at the N-terminus of bovine PRDX2, where a Cys-Val-Cys motif was identified. The expression of the six PRDXs in 22 bovine tissues has been studied by RT-PCR. Our results point out the ubiquity of the different PRDX transcripts in bovine tissues. The important conservation of the different PRDXs, the multiple processes they have been associated with, as well as the ubiquity of all the members of the family analyzed in this study for the first time altogether, suggest that they play a major role in the basal metabolism of mammalian cells.

L9 ANSWER 10 OF 15 MEDLINE on STN DUPLICATE 5

2003148414. PubMed ID: 12654475. Recombinant peroxiredoxin 5 protects against excitotoxic brain lesions in newborn mice. **Plaisant Frank** ; Clippe Andre; Vander Stricht Delphine; **Knoops Bernard;** **Gressens Pierre.** (INSERM E 9935 and Service de Neurologie Pediatrique, Hopital Robert-Debre, Paris, France. ) Free radical biology & medicine, (2003 Apr 1) 34 (7) 862-72. Journal code: 8709159. ISSN: 0891-5849. Pub. country: United States. Language: English.

AB The pathophysiology of brain lesions associated with cerebral palsy is multifactorial and likely involves excess release of glutamate and excess production of free radicals, among other factors. Theoretically, antioxidants could limit the severity of these brain lesions. Peroxiredoxins are a family of peroxidases widely distributed in eukaryotes and prokaryotes. Peroxiredoxin 5 (**PRDX5**) is a recently discovered mammalian member of this family of antioxidant enzymes that is able to reduce hydrogen peroxide and alkyl hydroperoxides. The

present study was designed to examine the neuroprotective effects of recombinant **PRDX5** against neonatal excitotoxic challenge in both in vivo and in vitro experiments. For in vivo experiments, mice (postnatal day 5) were injected intraneopallially with ibotenate acting on NMDA and metabotropic receptors, or S-bromowillardiine acting on AMPA-kainate receptors to produce excitotoxic stress and brain lesions. Systemically administered recombinant **PRDX5** provided protection against ibotenate-induced excitotoxic stress. Brain lesions of animals given ibotenate and **PRDX5** were up to 63% smaller than that given ibotenate alone. However, **PRDX5** provided no prevention from lesions induced with S-bromowillardiine. A mutated recombinant **PRDX5** that is devoid of peroxidase activity was also tested and showed no protection against lesions induced by either ibotenate or S-bromowillardiine. Two classical antioxidants, N-acetylcysteine and catalase-PEG, provided the same neuroprotective effect as **PRDX5.** For in vitro experiments, neocortical neurons were exposed to 300 microM NMDA alone, NMDA plus recombinant **PRDX5**, or NMDA, recombinant **PRDX5** and dithiothreitol, a classical electron donor for peroxiredoxins. Recombinant **PRDX5** plus dithiothreitol displayed a synergistic neuroprotective effect on NMDA-induced neuronal death. These findings indicate that reactive oxygen species production participates in the formation of NMDA receptor-mediated brain lesions in newborn mice and that antioxidant compounds, such as **PRDX5**, provide some neuroprotection in these models.

L9 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

2002:594988 Document No. 137:151800 Crystal structure of peroxiredoxin 5 and its use for design of structural homologues for treating oxidative-stress related disorders. Declercq, Jean-Paul; **Knoops, Bernard**; Evrard, Christine; Clippe, Andre; Van der Stricht, Delphine; **Bernard, Alfred** (Universite Catholique De Louvain, Belg.). PCT Int. Appl. WO 2002061063 A1 20020808, 101 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-EP890 20020129. PRIORITY: EP 2001-870016 20010130.

AB The present invention provides the crystal structure of peroxiredoxin 5 ( **PRDX5**), which allows to determine the key structural features of active binding pocket of **PRDX5.** The present invention relates to a crystal comprising a **PRDX5** protein in crystalline form that has the tetragonal space group symmetry P41 21 2. The invention further relates to a method for synthesizing a homolog of said crystal or an active binding site pocket , wherein said method comprises (a) providing the coordinates of the active binding site pocket of **PRDX5**, defined by residues of Table 2 and structure coordinates in Table 1, to a computer modeling system, (b) designing a homolog of said crystal or said active binding site pocket; (c) synthesizing said homolog, (d) optionally screening said homolog in a peroxidase activity assay for determining its catalytic activity, and (e) if desired, determining whether said compound inhibits oxidation in an antioxidant activity assay.

L9 ANSWER 12 OF 15 MEDLINE on STN DUPLICATE 6

2002657506. PubMed ID: 12417342. Expression and regulation of peroxiredoxin 5 in human osteoarthritis. **Wang Min Xia**; Wei Aiqun; Yuan Jun; Trickett Annette; **Knoops Bernard**; **Murrell George A C.** (Orthopaedic Research Institute, St George Hospital, University of New South Wales, Sydney, NSW, Australia. ) FEBS letters, (2002 Nov 6) 531 (2) 359-62. Journal code: 0155157. ISSN: 0014-5793. Pub. country: Netherlands. Language: English.

AB Reactive oxygen species (ROS) are implicated in the pathogenesis of osteoarthritis (OA). However, little is known about the antioxidant defence system in articular cartilage. We investigated the expression and regulation of peroxiredoxin 5 (**PRDX5**), a newly discovered thioredoxin peroxidase, in human normal and osteoarthritic cartilage. Our results show that human cartilage constitutively expresses **PRDX5** . Moreover, the expression is up-regulated in OA. Inflammatory cytokines tumour necrosis factor alpha and interleukin 1 beta contribute to this up-regulation by increasing intracellular ROS production. The present study suggests that **PRDX5** may play a protective role against oxidative stress in human cartilage.

L9 ANSWER 13 OF 15 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

2003:326944 Document No.: PREV200300326944. ANTIOXIDANT ENZYME PEROXIREDOXIN 5 IS EXPRESSED AT LOWER LEVELS IN NEURONS VULNERABLE TO CELL DEATH IN ALZHEIMER'S DISEASE. Landtmeters, M. [Reprint Author]; Alzate, L. [Reprint Author]; Brion, J. P.; **Knoops, B.** [Reprint Author]. Laboratory of Cell Biology, Universit Catholique de Louvain, Louvain-la-Neuve, Belgium. Society for Neuroscience Abstract Viewer and Itinerary Planner, (2002) Vol. 2002, pp. Abstract No. 784.4. http://sfn.scholarone.com. cd-rom.
Meeting Info.: 32nd Annual Meeting of the Society for Neuroscience. Orlando, Florida, USA. November 02-07, 2002. Society for Neuroscience.
Language: English.

AB Peroxiredoxin 5 (**PRDX5**) is a peroxidase of the mitochondrial thioredoxin system which is thought to play a major protective role against oxidative damages. Many neurological disorders, including Alzheimers disease (AD), are associated with oxidative stress and mitochondria have been implicated in such a process. In AD, the hippocampus is one of the first region of the brain to develop neuropathological lesions and is, in advanced cases, an heavily affected area. To determine whether the vulnerability of certain neuronal populations of the hippocampus could be due to a less efficient protection by the mitochondrial thioredoxin system, we analyzed by immunohistochemistry the expression of **PRDX5** in the hippocampus of adults rats, of normal control humans and of AD patients. Our results show that **PRDX5** is well expressed in neurons of CA4 and CA2/3 sectors, and of the subiculum. However, **PRDX5** immunoreactivity was weak in neurons of the CA1 sector and of the dentate gyrus. In AD brains, **PRDX5** expression in CA1 decreased or was totally absent. Moreover, we tested in COS-7 cells the protection conferred by **PRDX5** overexpression against oxidative stress induced by peroxides. At 100 M tert-butyl hydroperoxide, high expression of **PRDX5** decreased significantly apoptotic cell death. These results suggest that high levels of **PRDX5** may play an important protective role against oxidative stress. We conclude that the vulnerability of certain neuronal populations of the hippocampus in AD could be partly due to a weak expression of **PRDX5.**

L9 ANSWER 14 OF 15 MEDLINE on STN DUPLICATE 7

2001475436. PubMed ID: 11518528. Crystal structure of human peroxiredoxin 5, a novel type of mammalian peroxiredoxin at 1.5 A resolution. Declercq J P; Evrard C; Clippe A; Stricht D V; **Bernard A; Knoops B** . (Universite Catholique de Louvain, Unit of Structural Chemistry (CSTR), 1 place Louis Pasteur, Louvain-la-Neuve, B-1348, Belgium.. declercq@chim.ucl.ac.be) . Journal of molecular biology, (2001 Aug 24) 311 (4) 751-9. Journal code: 2985088R. ISSN: 0022-2836. Pub. country: England: United Kingdom. Language: English.

AB The peroxiredoxins define an emerging family of peroxidases able to reduce hydrogen peroxide and alkyl hydroperoxides with the use of reducing equivalents derived from thiol-containing donor molecules such as thioredoxin, glutathione, trypanothione and AhpF. Peroxiredoxins have been identified in prokaryotes as well as in eukaryotes. Peroxiredoxin 5 (**PRDX5**) is a novel type of mammalian thioredoxin peroxidase

widely expressed in tissues and located cellularly to mitochondria, peroxisomes and cytosol. Functionally, **PRDX5** has been implicated in antioxidant protective mechanisms as well as in signal transduction in cells. We report here the 1.5 A resolution crystal structure of human **PRDX5** in its reduced form. The crystal structure reveals that **PRDX5** presents a thioredoxin-like domain. Interestingly, the crystal structure shows also that **PRDX5** does not form a dimer like other mammalian members of the peroxiredoxin family. In the reduced form of **PRDX5**, Cys47 and Cys151 are distant of 13.8 A although these two cysteine residues are thought to be involved in peroxide reductase activity by forming an intramolecular disulfide intermediate in the oxidized enzyme. These data suggest that the enzyme would necessitate a conformational change to form a disulfide bond between catalytic Cys47 and Cys151 upon oxidation according to proposed peroxide reduction mechanisms. Moreover, the presence of a benzoate ion, a hydroxyl radical scavenger, was noted close to the active-site pocket. The possible role of benzoate in the antioxidant activity of **PRDX5** is discussed.


L9 ANSWER 15 OF 15 MEDLINE on STN DUPLICATE 8
2001329618. PubMed ID: 11396953. Antioxidant enzyme peroxiredoxin 5 is upregulated in degenerative human tendon. **Wang M X**; Wei A; Yuan J; Clippe A; **Bernard A**; **Knoops B**; **Murrell G A**
. (Orthopaedic Research Institute, St. George Hospital, University of New South Wales, 4-10 South Street, Sydney, New South Wales 2217, Australia. ) Biochemical and biophysical research communications, (2001 Jun 15) 284 (3) 667-73. Journal code: 0372516. ISSN: 0006-291X. Pub. country: United States. Language: English.
AB Peroxiredoxin 5 (**PRDX5**) is a novel thioredoxin peroxidase recently identified in a variety of human cells and tissues, which is considered to play an important role in oxidative stress protection mechanisms. However, little is known about its expression in tendon degeneration, a common and disabling condition that primarily affects older people, in which oxidative stress may be implicated. The present study demonstrated that normal human tendon expresses **PRDX5** and its expression is significantly increased in degenerative tendon. In addition, we have localized **PRDX5** to fibroblasts in normal tendon and to both fibroblasts and endothelial cells in degenerate tendon. The differential expression of **PRDX5** in normal and degenerate tendon shows that a thioredoxin peroxidase with antioxidant properties is upregulated under pathophysiological conditions and suggests that oxidative stress may be involved in the pathogenesis of tendon degeneration. **PRDX5** may play a protective role against oxidative stress during this pathophysiological process.


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=> s peroxiredoxin 5
L10         165 PEROXIREDOXIN 5

=> s l10 and homolog
L11           7 L10 AND HOMOLOG

=> dup remove l11
PROCESSING COMPLETED FOR L11
L12           7 DUP REMOVE L11 (0 DUPLICATES REMOVED)

=> d l12 1-7 cbib abs
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L12 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
2005:1075909 Document No. 143:361217 Cloning of human solid cancer antigens, and use for cancer diagnosis and therapy. Shimada, Hideaki; Tomonaga, Takeshi; Hiwasa, Takaki; Matsushita, Kazuyuki; Ochiai, Takenori; Nomura, Fumio; Takiguchi, Masaki (Medical Biological Laboratories Co., Ltd.,

Japan). PCT Int. Appl. WO 2005093063 A1 20051006, 262 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2005-JP6222 20050324. PRIORITY: JP 2004-95732 20040329.

AB This invention provides novel antigens useful in diagnosing solid tumors, encoding cDNAs, antibodies against these antigens and a method of diagnosing cancer using the same. Diagnostic kits comprising antibodies, probe or primer set for detecting those proteins or genes are also provided. Use of antibodies for cancer therapy is claimed. Twenty antigens not previously known to be tumor antigens were identified from colon cancer patients by two-dimensional electrophoresis and 19 antigens were identified from esophagus cancer patients by SEREX.

L12 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

2005:281854 Document No. 142:332482 Diagnostic method for brain damage-related disorders. Hochstrasser, Denis Francois; Sanchez, Jean-Charles; Lescuyer, Pierre; Allard, Laure (Universite De Geneve, Switz.; Lucas, Brian). PCT Int. Appl. WO 2005029088 A2 20050331, 92 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-GB50012 20040920. PRIORITY: GB 2003-22063 20030920; GB 2004-14089 20040623; GB 2004-19068 20040827.

AB A brain damage-related disorder is diagnosed in a subject by detecting at least one polypeptide, or a variant or mutant there« selected from A-FABP, E-FABP, PGP 9.5, GFAP, Prostaglandin D synthase, Neuromodulin, Neurofilament L, Calcyphosine, RNA binding regulatory subunit, Ubiquitin fusion degradation protein 1 **homolog**, Nucleoside diphosphate kinase A, Glutathione S transferase P, Cathepsin D, DJ-1 protein, **Peroxiredoxin 5** and Peptidyl-prolyl cis-trans isomerase A (Cyclophilin A) in a sample of body fluid taken from the subject.

L12 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

2005:182920 Document No. 142:258503 Secreted polypeptide species in human plasma, detection assays for smaller proteins and tryptic peptides, and expression profiles useful for disease diagnosis. Argoud-puy, Guilaine; Bederr, Nassima; Bougueleret, Lydie; Cusin, Isabelle; Mahe, Eve; Niknejad, Anne; Reffas, Samia; Rose, Keith; Saudrais, Cedric; Scherer, Andreas; Papoian, Ruben; Dengler, Uwe Jochen; Croft, Laurence James (Genova Ltd., Bermuda; Novartis Ag; Novartis Pharma GmbH). PCT Int. Appl. WO 2005019825 A2 20050303, 284 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-EP9323 20040819. PRIORITY: US 2003-2003/PV496966 20030820.

AB The invention relates to polypeptide species secreted in human plasma, isolated polynucleotides encoding such polypeptides, polymorphic variants thereof, and the use of said nucleic acids and polypeptides or compns. thereof for detection assays and disease diagnosis. An industrial-scale

method, involving sample pooling, is detailed for the anal. of smaller proteins (mol. weight less than about 40 kDa and mostly under 20 kDa),a nd thousands of peptides resulting from polypeptides can be identified from a single pool. Low abundance proteins such as leptin and ghrelin and peptides such as bradykinin, were clearly identified. By identifying the actual plasma polypeptide species, differences in mRNA processing and splicing, translation rate, mRNA stability, and posttranslational modifications are revealed, and plasma localization points to a novel, previously unknown function for the polypeptides of the invention. Peptides corresponding to 3 specific human plasma polypeptides (HPP) were identified and selected for functional characterization: esophageal cancer-related gene 2 (ECRG2), thymosin β4, and pancreastatin. Treatment of mice with these three HPP species resulted in gene expression profiles showing that these proteins would be useful in diagnosis treatment of cancer or hyperplasia-associated conditions, neurodegeneration or ion balance-associated diseases, and diseases associated with dysregulated serum glucose (e.g., diabetes) or metabolic disorders (e.g., amyloidosis).

L12 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
2005:394682 Document No. 142:445550 Gene expression profiles for the diagnosis and prognosis of breast cancer. Erlander, Mark; Ma, Xiao-Jun; Wang, Wei; Wittliff, James L. (Arcturus Bioscience, Inc. University of Louisville, USA). U.S. Pat. Appl. Publ. US 2005095607 A1 20050505, 40 pp. (English). CODEN: USXXCO. APPLICATION: US 2004-795092 20040305. PRIORITY: US 2003-2003/PV453006 20030307.
AB The invention relates to the identification and use of gene expression profiles, or patterns, suitable for identification of breast cancer patient populations with different survival outcomes. The gene expression profiles may be embodied in nucleic acid expression, protein expression, or other expression formats, and may be used in the study and/or determination of the prognosis of a patient, including breast cancer survival.

L12 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
2004:85983 Document No. 140:194431 Human prostate cancer marker genes associated with various metastatic stages identified by gene profiling, and related compositions, kits, and methods for diagnosis, prognosis and therapy. Schlegel, Robert; Endege, Wilson O. (Millennium Pharmaceuticals, Inc., USA). U.S. Pat. Appl. Publ. US 2004009481 A1 20040115, 131 pp. (English). CODEN: USXXCO. APPLICATION: US 2002-XA166883 20020611. PRIORITY: US 2001-2001/PV29728U 20010611; US 2002-2002/166883 20020611.
AB The invention relates to compns., kits, and methods for diagnosing, staging, prognosing, monitoring and treating human prostate cancers. A variety of marker genes are provided, wherein changes in the levels of expression of one or more of the marker genes is correlated with the presence of prostate cancer. In particular, three sets of the marker genes, corresponding to 11617 GenBank Accession Nos. (only 2168 new submissions) and 15 SEQ IDs, are identified by transcription profiling using RNA derived from clin. samples, that were expressed at least 2-fold or greater than the normal controls. Using TNM staging approach, these markers are divided to three groups, ones can be used to determine whether prostate cancer has metastasized, or is likely to metastasize, to the liver (M stage); ones can be used to determine whether prostate cancer has metastasized, or is likely to metastasize, to the bone (M stage); and ones can be used to determine whether prostate cancer has metastasized, or is likely to metastasize, to the lymph nodes (N stage and/or M stage). The invention also relates to a kit for assessing the specific type of metastatic prostate cancer, e.g., cancer that has metastasized to the liver, bone or lymph nodes. [This abstract record is one of three records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

L12 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
2002:594988 Document No. 137:151800 Crystal structure of **peroxiredoxin 5** and its use for design of structural

homologues for treating oxidative-stress related disorders. Declercq, Jean-Paul; Knoops, Bernard; Evrard, Christine; Clippe, Andre; Van der Stricht, Delphine; Bernard, Alfred (Universite Catholique De Louvain, Belg.). PCT Int. Appl. WO 2002061063 A1 20020808, 101 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-EP890 20020129. PRIORITY: EP 2001-870016 20010130.

AB The present invention provides the crystal structure of **peroxiredoxin 5** (PRDX5), which allows to determine the key structural features of active binding pocket of PRDX5. The present invention relates to a crystal comprising a PRDX5 protein in crystalline form that has the tetragonal space group symmetry P41 21 2. The invention further relates to a method for synthesizing a **homolog** of said crystal or an active binding site pocket , wherein said method comprises (a) providing the coordinates of the active binding site pocket of PRDX5, defined by residues of Table 2 and structure coordinates in Table 1, to a computer modeling system, (b) designing a **homolog** of said crystal or said active binding site pocket; (c) synthesizing said **homolog**, (d) optionally screening said **homolog** in a peroxidase activity assay for determining its catalytic activity, and (e) if desired, determining whether said compound inhibits oxidation in an antioxidant activity assay.

L12 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

2002:923673 Document No. 138:266659 Gene expression profiling of androgen deficiency predicts a pathway of prostate apoptosis that involves genes related to oxidative stress. Pang, See-Tong; Dillner, Karin; Wu, Xuxia; Pousette, Ake; Norstedt, Gunnar; Flores-Morales, Amilcar (Department of Molecular Medicine, Karolinska Institute, Karolinska Hospital, Stockholm, 171 76, Swed.). Endocrinology, 143(12), 4897-4906 (English) 2002. CODEN: ENDOAO. ISSN: 0013-7227. Publisher: Endocrine Society.

AB Androgens are critical for prostate development, growth, and functions. In general, they support proliferation and prevent cell death of prostatic epithelial cells. Here, we studied changes of gene expression after castration and testosterone replacement therapy in the rat ventral prostate using cDNA microarrays anal. We could identify 230 genes that were regulated in either exptl. condition. Using hierarchical clustering anal., different groups of genes could be detected according to their expression pattern. This enabled us to distinguish the putative androgen-responsive genes from the secondary-responsive ones. Among genes that altered during castration and testosterone replacement, a set of oxidative stress-related genes, including thioredoxin, **peroxiredoxin 5**, superoxide dismutase 2, glutathione peroxidase 1, selenoprotein 15 kDa, microsomal glutathione-S-transferase, glutathione reductase, and epoxide hydrolase, were changed by castration. We hypothesize that modulation of redox status can be a factor of relevance in androgen withdrawal-induced prostate apoptosis. In selective cases, quant. RT-PCR was used to confirm changes in gene expression. Immunohistochem. was performed to detect thioredoxin and ezrin. Both of these were detected in the prostate and seem to be regulated in a similar manner as shown by gene expression anal. In conclusion, gene expression profiling provides a unique opportunity for understanding the mol. mechanisms of androgen actions in prostate gland.

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L13 0 L10 AND REDUCTANT

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L14 9 L10 AND ELECTRON DONOR

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L15 ANSWER 1 OF 4 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 1
2003269233 EMBASE The tetrameric structure of Haemophilus influenza hybrid Prx5 reveals interactions between **electron donor** and acceptor proteins. Kim S.J.; Woo J.R.; Hwang Y.S.; Jeong D.G.; Shin D.H.; Kim K.; Ryu S.E.. S.E. Ryu, Ctr. Cell. Switch Protein Struct., Korea Res. Inst. of Biosci./Biotech., 52 Euh-eun-dong, Yusong-gu, Daejon 305-806, Korea, Republic of. ryuse@mail.kribb.re.kr. Journal of Biological Chemistry Vol. 278, No. 12, pp. 10790-10798 21 Mar 2003.
Refs: 42.
ISSN: 0021-9258. CODEN: JBCHA3
Pub. Country: United States. Language: English. Summary Language: English.
ED Entered STN: 20030731
AB Cellular redox control is often mediated by oxidation and reduction of cysteine residues in the redox-sensitive proteins, where thioredoxin and glutaredoxin (Grx) play as **electron donors** for the oxidized proteins. Despite the importance of protein-protein interactions between the **electron donor** and acceptor proteins, there has been no structural information for the interaction of thioredoxin or Grx with natural target proteins. Here, we present the crystal structure of a novel Haemophilus influenza peroxiredoxin (Prx) hybrid Prx5 determined at 2.8-A resolution. The structure reveals that hybrid Prx5 forms a tightly associated tetramer where active sites of Prx and Grx domains of different monomers interact with each other. The Prx-Grx interface comprises specific charge interactions surrounded by weak interactions, providing insight into the target recognition mechanism of Grx. The tetrameric structure also exhibits a flexible active site and alternative Prx-Grx interactions, which appear to facilitate the electron transfer from Grx to Prx domain. Differences of **electron donor** binding surfaces in Prx proteins revealed by an analysis based on the structural information explain the **electron donor** specificities of various Prx proteins.

L15 ANSWER 2 OF 4 MEDLINE on STN DUPLICATE 2
2003148414. PubMed ID: 12654475. Recombinant **peroxiredoxin 5** protects against excitotoxic brain lesions in newborn mice. Plaisant Frank; Clippe Andre; Vander Stricht Delphine; Knoops Bernard; Gressens Pierre. (INSERM E 9935 and Service de Neurologie Pediatrique, Hopital Robert-Debre, Paris, France. ) Free radical biology & medicine, (2003 Apr 1) 34 (7) 862-72. Journal code: 8709159. ISSN: 0891-5849. Pub. country: United States. Language: English.
AB The pathophysiology of brain lesions associated with cerebral palsy is multifactorial and likely involves excess release of glutamate and excess production of free radicals, among other factors. Theoretically, antioxidants could limit the severity of these brain lesions. Peroxiredoxins are a family of peroxidases widely distributed in eukaryotes and prokaryotes. **Peroxiredoxin 5** (PRDX5) is a recently discovered mammalian member of this family of antioxidant enzymes that is able to reduce hydrogen peroxide and alkyl hydroperoxides. The present study was designed to examine the neuroprotective effects of recombinant PRDX5 against neonatal excitotoxic challenge in both in vivo and in vitro experiments. For in vivo experiments, mice (postnatal day 5) were injected intraneopallially with ibotenate acting on NMDA and metabotropic receptors, or S-bromowillardiine acting on AMPA-kainate receptors to produce excitotoxic stress and brain lesions. Systemically administered recombinant PRDX5 provided protection against ibotenate-induced excitotoxic stress. Brain lesions of animals given

ibotenate and PRDX5 were up to 63% smaller than that given ibotenate alone. However, PRDX5 provided no prevention from lesions induced with S-bromowillardiine. A mutated recombinant PRDX5 that is devoid of peroxidase activity was also tested and showed no protection against lesions induced by either ibotenate or S-bromowillardiine. Two classical antioxidants, N-acetylcysteine and catalase-PEG, provided the same neuroprotective effect as PRDX5. For in vitro experiments, neocortical neurons were exposed to 300 microM NMDA alone, NMDA plus recombinant PRDX5, or NMDA, recombinant PRDX5 and dithiothreitol, a classical **electron donor** for peroxiredoxins. Recombinant PRDX5 plus dithiothreitol displayed a synergistic neuroprotective effect on NMDA-induced neuronal death. These findings indicate that reactive oxygen species production participates in the formation of NMDA receptor-mediated brain lesions in newborn mice and that antioxidant compounds, such as PRDX5, provide some neuroprotection in these models.

L15 ANSWER 3 OF 4 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
2002:510291 Document No.: PREV200200510291. Advances in our understanding of peroxiredoxin, a multifunctional, mammalian redox protein. Fujii, Junichi [Reprint author]; Ikeda, Yoshitaka. Department of Biochemistry, Yamagata University School of Medicine, 2-2-2 Iidanishi, Yamagata, 990-9585, Japan. jfujii@med.id.yamagata-u.ac.jp. Redox Report, (2002) Vol. 7, No. 3, pp. 123-130. print.
ISSN: 1351-0002. Language: English.

AB Organisms living under aerobic conditions have developed various anti-oxidative mechanisms to protect them from damage by reactive oxygen species (ROS). A novel family of anti-oxidative proteins, designated as peroxiredoxin (Prx), has been identified in the past two decades and currently comprises six members in mammals. They share a common reactive Cys residue in the N-terminal region, and are capable of serving as a peroxidase and involve thioredoxin and/or glutathione as the **electron donor.** Prx1 to Prx4 have an additional Cys residue in the conserved C-terminal region, and are cross members as judged by the amino acid sequence similarity. Prx5 also contains an additional Cys in its C-terminal region which is less conserved. On the other hand, Prx6 has only one unique Cys. These Prx family members are distributed in the cytosol, mitochondria, peroxisome and plasma, all of which are potential sites of ROS production. In addition to their role as a peroxidase, however, a body of evidence has accumulated to suggest that individual members also serve divergent functions which are associated with various biological processes such as the detoxification of oxidants, cell proliferation, differentiation and gene expression. It would be expected that these functions might not necessarily depend on peroxidase activity and, therefore, it seems likely that the divergence is due to unique molecular characteristics intrinsic to each member. A comparative study of the divergence would lead to a better understanding of the biological significance of the Prx family.

L15 ANSWER 4 OF 4 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
1999:391394 Document No.: PREV199900391394. Characterization of the murine gene encoding 1-Cys peroxiredoxin and identification of highly homologous genes. Lee, Tae-Hoon; Yu, Seong-Lan; Kim, Sun-Uk; Kim, Yong-Man; Choi, Inpyo; Kang, Sang Won; Rhee, Sue Goo; Yu, Dae-Yeul [Reprint author]. Korea Research Institute of Bioscience and Biotechnology, Yusong, Taejon, 305-600, South Korea. Gene (Amsterdam), (July 8, 1999) Vol. 234, No. 2, pp. 337-344. print.
CODEN: GENED6. ISSN: 0378-1119. Language: English.

AB A new type of peroxiredoxin, named 1-Cys peroxiredoxin (1-Cys Prx), reduces hydrogen peroxide with the use of electrons from unidentified **electron donor**(s). We have isolated the mouse gene encoding 1-Cys Prx (CP-3) and shown that it is comprised of five exons and four introns. Analysis of 5' flanking regions revealed binding sequences of several putative transcription factors such as Sp1, Pit-1a, c-Jun, c-Myc and YY1. It is noticeable that several potential Sp1 binding sites assigned the -60 through -96 bp from putative transcription initiation

site. The gel shift assays showed that Sp1 and Pit-1a bind specifically to each binding site in 1-Cys Prx promoter. We also isolated two highly related genes such as CP-2 and CP-5. These genes are encoded by single exons, and show 85% of nucleotide sequence homology with the CP-3. The structural features of these genes suggest that they might be intronless genes derived from the CP-3 by the mechanism involving retrotransposition. Inaddition, our data suggest that they are inserted to a specific site of the mouse L1 repetitive element. The 1-Cys Prx was actively transcribed in a variety of adult tissues as well as in the developing embryos. These results suggest that only the 1-Cys Prx gene might be relevant for studying the function of the 1-Cys Prx in the murine system.

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| FULL ESTIMATED COST | 162.40 | 162.61 |

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